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JULY 1936

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH
DEARBORN STREET, CHICAGO, ILLINOIS ANNUAL SUBSCRIPTION, \$8 00

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Archives of Dermatology and Syphilology

VOLUME 34

JULY 1936

NUMBER 1

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DERMATOPHYTOSIS AND DERMATOPHYTIDS

WITH PARTICULAR REFERENCE TO THE DIFFERENTIAL DIAGNOSIS OF
DYSHIDROSIFORM ERUPTIONS OF THE HANDS AND FEET

FRED WISE, M D

AND

JACK WOLF, M D

NEW YORK

Interest in the broad subject embraced by the term dyshidrosiform eruptions of the hands and feet has in recent years acquired a tremendous impetus as a result of the discovery that a primary fungous infection of the skin of the feet may give rise to secondary vesicular and other inflammatory lesions on the hands and on other parts of the body¹

The incidence of superficial mycotic lesions of the skin has become so widespread in most parts of the world, and especially in this country, that opportunities for study and investigation are unlimited, advantage has been taken of these opportunities by scores of clinical observers and laboratory investigators, with the result that more light is constantly thrown on the various phases and problems connected with dyshidrosiform dermatoses as a whole. These investigations have led to ramifications embracing the fields of atopy, allergy, immunology, mycology, biologic chemistry, serology, pharmacology and chemistry.

With this in mind, we deemed it expedient to restrict ourselves in this address to certain narrower phases of the subject and decided to deal with certain aspects pertaining particularly to the differential diagnosis of a group of dyshidrosiform dermatoses.

Included in this group are the following:

1 Eruptions due to superficial mycotic infections—infections with *Trichophyton*, *Epidermophyton* and yeasts

Read at the Seventh Annual Spring Clinical Conference of the Dallas Southern Clinical Society, Dallas, Texas, March 18 1935

The publication of this article was delayed for many months by a discussion of the nomenclature of fungous diseases in general, which the ARCHIVES was trying to unravel.

¹ Williams, C M. Enlarging Conception of Dermatophytosis, *Arch Dermat & Syph* 15:451 (April) 1927

2 Eruptions of secondary nature resulting from primary fungous foci—epidermophytids, monilids and trichophytids

3 Eruptions caused by exogenous irritants These fall in the category of dermatitis venenata, occupational dermatoses, trade eczemas, industrial dermatoses, dermatitis eczematosa and so forth These eruptions are encountered most frequently among dyers, furriers, painters, tanners, leather-workers, barbers, hair-dressers, photographers, workers in ammunition and rubber factories, and in the electrical and oil industries, printers, typesetters, persons who handle food, florists, chemists, druggists, surgeons, dentists, nurses and persons in scores of other occupations and professions

4 Vesicular eruptions of unknown cause—"eczema," dermatitis eczematosa and pompholyx

5 Toxic eruptions caused by drugs, foods, etc

The fact is known to all dermatologists that the dyshydrosiform eruptions representing these five groups are, with certain exceptions, clinically indistinguishable from one another in a large proportion of unselected patients We stress the term unselected patients, because this statement evidently would not be applicable to a group of patients employed, for example, in an ammunition plant, a rubber factory or a fur-dyeing establishment, we have in mind rather the general run of patients encountered in every-day private and clinic practice

Attempts to differentiate the vesicular palmar and plantar dermatoses by means of clinical criteria alone have not met with success A few dermatologists maintain that while clinical differentiation is difficult it should not be entirely ignored, as it is by many Scholtz,² for instance, who published a paper three years ago in which he dealt with the morphologic features of dyshydrosiform eruptions, remarked "The diagnostic value of the morphologic differences between mycotic dyshydrotic lesions and those of systemic dyshydrosis has been generally underestimated by dermatologists and completely ignored by the protagonists of epidermophytids" He expressed the opinion that if more attention were given to the details of the clinical changes it might be helpful in arriving at a correct diagnosis Varying opinions along the same lines of thought were expressed by Mitchell³ of Chicago and Lehmann⁴ of San Antonio Mitchell said "I do not pretend to be able to determine by inspection what is mycotic and what is not, and the only way this can be determined is by making strenuous efforts to find out whether they are mycotic"

2 Scholtz, Moses Epidermophytids as a Clinical Conception, *Arch Dermat & Syph* 25 812 (May) 1932

3 Mitchell, J H Amycotic Dermatoses Simulating Ringworm and Erosio Interdigitalis Blastomycetica, *Arch Dermat & Syph* 19 659 (April) 1929

4 Lehmann, C F Acute Vesicular Eruptions of the Hands and Feet, *Arch Dermat & Syph* 21 449 (March) 1930

Relative to this aspect of the subject, our own experience has effected a dubious attitude and guarded expression of opinion. We do believe, however, that the morphologic features of a dermatophytid can be faithfully mimicked by lesions due to almost any number and variety of irritants, both exogenous and endogenous, and that when the patient who presents a vesicular eruption on the hands of indeterminate and obscure cause happens also to be afflicted with ringworm infection of the toes, then indeed is confusion worse confounded.

This brings us to the declaration of an opinion which we think is shared by the majority of dermatologists in this country, namely, that it is futile to shut one's eyes to the fact that among the rank and file of practitioners the tendency to make false interpretations of these simultaneous eruptions on the feet and on the hands has become far too prevalent. To state the case bluntly, innumerable wrong diagnoses are constantly made and improper therapy is prescribed in cases of dyshydrosiform eruptions and have been ever since the "athletes' foot" propaganda came into its own, flourished and attained full bloom. The technic of many practitioners is to cast a glance at the vesicular eruption on the patient's hands and say to himself, "Ah! another case of ringworm infection," and then to the patient, "Let me see your feet. Yes, I thought so! You have ringworm of the feet, and the blisters on your hands are caused by the same parasite." This explanation is delightfully simple, all it lacks is confirmation.

It seems paradoxical, but is nevertheless true, that those who have the most experience with this class of dermatoses are those who require the most time to obtain the patient's complete history, to perform the essential microscopic and cultural investigations, to delve into the patient's atopic, allergic and immunologic status and to ascertain his response to various remedies—in short, to arrive at the correct diagnosis and prescribe the right remedy, as against making a wrong "snap" diagnosis and prescribing the wrong remedy.

Try as hard as we may, we find it difficult to refrain from quoting that hackneyed phrase about the medical pendulum, with its nasty habit of swinging either too much to the right or too much to the left. If one accepts the dictum of a number of authoritative observers who believe that between 70 and 90 per cent—even 100 per cent—of dyshydrosiform eruptions on the hands and feet exclusive of those definitely evoked by exogenous irritants originate from fungous infections, one has still to deal with a fairly conspicuous group of patients whose eruptions can be classed neither as contact dermatitis nor as fungous infection. This leaves one, figuratively speaking, with several stepchildren whose progenitors are either under suspicion or wholly unknown.

PRESENT STATUS OF DERMATOPHYTOSIS AND DERMATOPHYTIDS

Much progress from both a clinical and a laboratory standpoint has been made in the study of fungous diseases within the last decade. Additions to the knowledge have been the burden of numerous communications in the foreign and American literature. It might be well to take stock, to review these steps forward, to correlate the findings and to evaluate critically the new contributions.

For the purpose of this presentation it might be best to start with a brief review of the etiology, symptomatology and pathology of dermatophytosis and dermatophytids.

In the study of a large mass of material at the New York Post-Graduate Medical School and Hospital, the organisms most frequently encountered on the feet were *Trichophyton gypseum*, *Trichophyton interdigitale* and *Monilia*. Of course, numerous other species of *Epidermophyton*, *Microsporon* and *Achorion* were found but they account for only a small percentage of the cases.

Fungi are ubiquitous. They live in the horny layer of the skin, and any factor or factors which favor maceration of the skin provide an excellent culture medium for the growth and propagation of the organisms. Moisture, and this is important from the standpoint of therapy, is therefore an outstanding contributory cause of fungous infection. It matters little whether the moisture is that of hyperhidrosis or of the bath, shower or swimming pool. The greatest opportunity for infection occurs wherever large groups of people meet and where insufficient prophylaxis against infection is taken, as at athletic clubs, gymnasiums and bath-houses.

The severity of the infection depends on many factors but primarily on the allergic response of the individual person to his infection. Of this we shall have more to say later.

The clinical appearance of tinea of the hands and feet is well known. There are the white, sodden epidermis, most frequently encountered between the fourth and fifth toes, the vesicular and bullous lesions found especially on the palms and soles and on the lateral surfaces of the fingers and feet, and the erythematous, dry, fissured, scaling eczematous areas found on both the hands and the feet. The hyperkeratotic type occurs less frequently. In tinea of the feet the toe-nails are most often involved, and any nail which lacks luster, even though it appears normal otherwise, will probably yield fungi on microscopic or cultural examination. Nails which are deformed, which show alterations in color or which present such changes as subungual hyperkeratosis are frequently involved. The infected toe-nail is said to play a not inconsiderable rôle in the production of recurrences.

The histopathology of dermatophytosis and of the dermatophytids is the histopathology of eczema. There are no tinctorial, morphologic or cellular changes which differ from those found in eczema.

In a great percentage of cases in which both the hands and the feet are involved and in which diligent search, both microscopic and cultural, is made, one finds no causative organism in the lesions on the hands. This fact led Williams to suggest that in such cases one is dealing with dermatophytosis of the feet and dermatophytids of the hands, hemogenous lesions of an allergic nature secondary to the primary lesions on the feet. These ids find their analogy in the trichophytid which appears in deep tinea infection, such as kerion, and also in the tuberculids. In 1929 Peck published experimental proof of Williams' original observation. By infecting the toes of previously unaffected persons and producing trauma by friction between the toes he caused vesicular eruptions to appear on the hands which were typical "ids." The hands appear to be a *locus minoris resistentiae* for the development of these secondary lesions.

The development of the trichophytid depends primarily on two factors, namely, (1) altered reactivity of the skin, i. e., allergy, and (2) the dissemination of the fungi or their products, or possibly both the fungi and the products combined, to the site of the "id." The altered reaction of the skin to fungi and their products is the allergy of infection, and for the sake of clarity we shall compare it with the immunologic reactions in another disease, tuberculosis. This altered reactivity depends on previous infection with fungi, and it can be demonstrated by the intradermal injection of toxins from fungi (trichophytin). This is analogous to the first infection with the tubercle bacillus and the demonstration of altered reactivity by the injection of tuberculin. This altered reactivity of the skin is responsible for the appearance of the "id," for the trichophytid (or monilid) is the result of an inflammatory response of the skin to the trichophytic (or *Monilia*) antigen.

In any discussion as to whether the "id" is due to the fungi or to their products (or to both), one is treading on debatable ground. Bloch was able to produce lesions resembling "ids" in animals by the injection of trichophytin. Jadassohn grew fungi repeatedly in cultures of the blood of cutaneously infected animals. These cultures, however, gave positive results in the early postinfectious period, and the fungi might have been forced into the blood stream by mechanical means. Sulzberger continued this work and demonstrated that a second phase, with numerous positive cultures of the blood, followed the first, postinfectious, phase with its succeeding negative phase. It is probable that the appearance of the "id" is coincidental with an infection in the blood stream with fungi from the feet. There is added proof in the occasional

positive culture of the blood reported for human beings Ambrosoli reported 2 positive cultures of 1,269 in a study of 700 cases of trichophytic disease The difficulties in obtaining positive cultures of the blood in sporadic specimens of a limited quantity of blood must be obvious

In this connection we call attention to the work of Ayres and Anderson These authors were able to show that from 4 to 8 per cent of serum from a person with true "id" when incorporated in Sabouraud's medium will inhibit the growth of fungi isolated from the primary lesion This does not hold true for *Cryptococcus*, pleomorphic forms of *Epidermophyton* or *Monilia*, nor does it hold true in instances of eruptions on the hands which are due to irritants, hypersensitivity or local infection with fungi This work, if confirmed, will add a helpful test to the armamentarium of the dermatologist in the differential diagnosis of dyshidrosiform eruptions

CHEIROPOMPHOLYX

Present Status—From the standpoint of pathogenesis and histopathology it is believed by the great majority of modern dermatologists that true palmar and plantar dyshidrosis, i e, an eruption caused primarily by a disorder of the sweat apparatus in these regions, does not exist (Such conditions as sudamina, miliaria crystallina and hydrocystoma do not fall into this category and are not pertinent to the present discussion)

The subject of cheiropompholyx was recently discussed in extenso in two articles in the *British Journal of Dermatology and Syphilis* by McLachlan and Brown⁵ and Muende⁶

In a series of cases which they studied the first-named authors found that "approximately 15 per cent of cheiropompholyx eruptions belong to the eczema, asthma and hay-fever group, and that there is a definite hereditary predisposition to eruptions of the allergic type"

A typical example was reported in a case of a woman aged 27

The patient suffered from urticaria, off and on, all her life In addition she had two or three attacks of angioneurotic edema She had also suffered, during her twenties, from attacks of cheiropompholyx with typical sago-grain vesicles The family history is as follows Maternal grandmother suffered from eczema Her paternal uncle suffered from asthma, and her paternal great-grandfather from hay-fever The patient herself is subject to urticaria, angioneurotic edema, bilious attacks after partaking of certain food, dysmenorrhea and finally cheiropompholyx

5 McLachlan, A D, and Brown, W H Cheiropompholyx, *Brit J Dermat* 46 457 (Nov) 1934

6 Muende, I Cheiropompholyx, *Brit J Dermat* 46 479 (Nov) 1934

The authors cited several cases in which more than one member of an atopic family group suffered simultaneously from this eruption, and they stated the belief that the inborn hereditary factor has been overlooked in cases of cheiropompholyx and that they had enough evidence to justify them in pointing out its importance

With this point of view we are in full accord. We have had the opportunity to observe two members of a family and, in one instance, a neurotic mother and her two neurotic daughters who had vesicular eruptions of the palms and lateral surfaces of the fingers and in whose cases the diagnosis of contact dermatitis, primary local fungous infection, trichophytid, monilid or idiopathic eczema did not seem to be applicable, despite the great latitude in the choice of diagnosis in such cases. Peck, in his paper on dermatophytosis, mentioned conditions which he could not classify under the head either of dermatophytid or of eczema and which he thought might be examples of true dyshidrosis. A still greater latitude in the field of clinical diagnostic excursions has been made available by the assumption that bacteria, acting either exogenously or endogenously, are capable of producing similar dyshidrosiform eruptions, as well as "bacteriids," in a sense analogous to mycosids and tuberculids. However, a number of observers, among whom are Sabouraud, Whitfield, Sicoli and Scholtz, still adhere to the conception of cheiropompholyx as a clinical entity of nonparasitic nature.

We have had 2 patients under observation in whom the ingestion of orange juice evoked vesicular lesions resembling sago grains on the palms and fingers. Manual contact with oranges or orange juice, the existence of ringworm, infection with *Monilia* and eczema could be fairly definitely ruled out. The eruption simulated trichophytids. Thus one is constrained to recognize that certain dyshidrosiform eruptions are at times encountered which apparently do not lend themselves to classification with contact dermatitis, local fungous infections, mycosids, bacteriids and "eczema." Notwithstanding the fact that the histopathologic changes in this group are practically identical with those occurring in dyshidrosiform eruptions of known etiology and despite the almost universally accepted view that disorders of the sweat apparatus are not causative factors, one is apparently still confronted with a condition to which the name cheiropompholyx has clung since 1871.

It is of interest to note that both Jadassohn and Darier have placed this condition in the category of eczema, a classification which the majority of British dermatologists regard as unsatisfactory. While it seems to us that the arguments in favor of the individuality of pompholyx are propounded by implication rather than by analysis, we still believe that the moment to drop the term pompholyx from the nomenclature has not arrived.

Pathogenesis—McLachlan and Brown⁵ lay considerable stress on neurogenic and endocrine-sympathetic factors in the etiology of cheiropompholyx. They stated

These causal factors have been noted by comparatively few writers, and seem to have been neglected. We would like to draw attention to their importance, for they occupy a definite place in our series. Nervous influences in relation to diseased states have within recent times become accepted as important aetiological factors, particularly in certain dermatoses, e g, neuro-dermatitis, alopecia, urticaria, eczema, etc, and there is every reason for believing that there is a neurogenic factor in certain cases of cheiropompholyx. The suddenness of onset is in itself suggestive of a nervous cause. Tilbury Fox records the probability of a nervous factor in cheiropompholyx, stating that "some patients were prostrated with mental anxiety and worry and were speedily exhausted." Becker, in his article on dermatoses associated with neuro-vascular instability, mentions neurogenic dyshidrosis, and says the nervous factor has been overlooked. O'Donovan observes that cheiropompholyx is often seen after nervous strain, worry or shock, while Martin from a personal experience emphasizes this point. In several of our cases the nervous element was the dominant one. In one case especially, which was under observation for twelve years, the nervous factor was particularly evident. The patient was a telephone operator, very nervous and highly strung, who stated emphatically that the eruption originally started after a local injury by a telephone wire, but that the subsequent attacks were associated with worry or nervous strain. Another case which may be cited is as follows:

Female, aged 15 years, dispatch girl. Thin and exhausted looking, and definitely neurotic in type. She states that previous to the onset of the eruption she had been extremely busy, and had worked after hours for many weeks. She exhibited a very decided tremor in both hands, and her reflexes were all exaggerated. She suffered from headaches and sleeplessness. No fungus was found, and no other evidence to account for her condition.

The association of cheiropompholyx with endocrine disturbances is difficult to assess, but the relationship between the two has been so close in a number of instances that it cannot be ignored. This has been commented upon by other writers. Pregnancy, menstruation and the menopause coincided with the attacks in 21 of our cases.

In several cases the attacks followed within 2 to 4 weeks of parturition, and in others were closely related to the menstrual period, or originated about the menopause. Lehmann recalls a case recurring a few days before each period, especially in hot weather. Further evidence of endocrine disturbance or the nervous factor is found in two patients who showed definite enlargement of the thyroid gland with a slight degree of exophthalmos, and in one case a very decided goitrous family history. The goitrous factor has been commented upon by Wile, who records a group of cases of non-parasitic cheiropompholyx clinically indistinguishable from ringworm. Living in the great goitre belt, he found many cases associated with exophthalmic goitre, which inclined him to believe that they were of neurogenic origin.

Among other modern investigators, Muende⁶ has upheld the conception of true dyshidrosis as a disease entity. In tabulating the funda-

mental signs and symptoms he adopted those propounded and agreed on by both Hutchinson and Fox. We quote Muende as follows:

1 The rash is preceded by a sense of increased discomfort in the parts to be affected.

2 The eruption then appears spontaneously and symmetrically on both hands without any antecedent erythema, has somewhat deeply placed minute flattish vesicles, which resemble sago-grains, embedded in the skin.

3 These vesicles appear scattered, at times irregularly, but at others in small groups along the sides of the fingers and also on the palms.

4 In severe cases these vesicles may coalesce to form large bullae.

5 The eruption undergoes spontaneous resolution without rupture of the vesicles, and

6 The condition tends to recur.

If we adhere rigidly to this description, as indeed we ought, when discussing a case of cheiropompholyx, it will soon become evident that the disease cannot be attributed to eczematous eruptions of exogenous origin, or wholly to infection with organisms, either mycotic or bacterial.

Muende expressed the opinion that there is a group of vesicular eruptions in which an infective origin cannot be incriminated nor can any exogenous or definite endogenous factor be observed. Sweating need not be a special feature in these cases, nor are the attacks related to hot weather. The patients are usually worried and overworked, but Muende did not care to suggest the mechanism producing the eruption.⁶

Rajka and several French writers have described cases of eruptions due to infection with the streptococcus or the staphylococcus, but the eruptions had no resemblance to true cheiropompholyx, corresponding rather to vesicular dermatoses caused by coccic-infection.⁶ We have examined patients who had vesicular eruptions on the hands, the clinical course and appearance of which seemed to justify the diagnosis of pompholyx rather than any other designation. Some of these eruptions might be due to sensitization to various foods or to such drugs as iodine and the salicylates.

From the foregoing statements the inference may be drawn that before the description of trichophytids and monilids—particularly of the palmar surfaces—pompholyx, as the name is interpreted in this country, had been recognized as a disease entity of nonparasitic nature. In England the name cheiropompholyx is applied to palmar and plantar vesicular eruptions in general, with qualifying adjectives, such as fungous, toxic, parasitic and nonparasitic. In American textbooks, even in those published within the past year pompholyx is described as a nonparasitic disease.

Since the facts regarding the allergic manifestations of the superficial mycoses, especially those expressed by vesicular palmar eruptions, have become generally known to American dermatologists, pompholyx has existed in what might be called a state of suspended animation.

DIFFERENTIAL DIAGNOSIS

If one assumes that efforts at purely clinical differentiation are of little practical value save in exceptional instances and that the most painstaking questioning of the patient with respect to external contacts, sensitization to certain foods and drugs, his occupation or profession, and his hobbies or participation in sports and games of various kinds offers no clue to possible etiologic factors, one has recourse to the following diagnostic procedures

1 One can search for the causative factor by means of patch tests, to determine epidermal sensitization to one or several allergens with which the patient might come in contact. Not only is this procedure applicable in cases of trade eczema and occupational dermatitis, but, as has been demonstrated,⁷ it may prove of value in identifying conditions suspected of being trichophytids. In certain cases of ringworm infection a patch test with trichophytin resulted in a reaction of the eczematous type, and histologic examination of these reactions showed typical spongiosis and intra-epidermal vesicles. This proves that products of fungi may elicit eczematous eruptions in hypersensitive skin in the same manner as do innumerable substances that play a causative rôle in industrial dermatoses. In children below the age of 5 years, in whom infection with *Epidermophyton* is comparatively rare in our experience, the patch test with trichophytin would seem to be of considerable diagnostic value. Unfortunately, from the practical standpoint the test does not hold good in adults on account of the widespread incidence of epidermophytosis of the feet in the adult population.

2 One can search for the causative factor by means of intradermal tests with extracts of trichophytin and oidiomycin. As pointed out by Jadassohn, by Bloch and his pupils and by many other investigators, this test is also of only limited diagnostic value for the reasons previously mentioned with respect to the patch test. The same limitations apply to the tuberculin test. It has been demonstrated⁸ that oidiomycin, the extract of *Monilia albicans*, in the majority of patients causes a positive intradermal reaction of the late papular type analogous to that evoked by trichophytin and tuberculin. There exists a sharp immunologic separation between hypersensitivity to trichophytin and hypersensitivity to oidiomycin, for sensitizations caused by the *Monilia* group and those caused by the *Epidermophyton* group seem to be specific for each group and are not immunologically related. Despite these indi-

7 Sulzberger, M. B., and Lewis, G. M. Trichophytin Hypersensitiveness Demonstrated by Contact Tests, *Arch. Dermat. & Syph.* 22: 410 (Sept.) 1930.

8 Kerr, P. S., Pascher, F., and Sulzberger, M. B. *Monilia* and *Trichophyton* Extracts. Their Combined Use in Eczematous Ringworm (Dermatophytosis and Dermatophytids), *J. Allergy* 5: 288 (March) 1934.

vidual specific reactions, the tests are of only limited value in adult patients with dyshidrotic eruptions, but they should prove of considerable value in cases of vesicular eruptions of the hands and feet in young children. It has been demonstrated that most persons possess a cutaneous hypersensitivity to oidiomycin and that some patients who have no evidence of present or past eruptions caused by *Monilia* exhibited a high degree of hypersensitivity to intradermal injections of oidiomycin. Therefore, as is the case with trichophytin and tuberculin, the reaction to the oidiomycin test is not diagnostic. It is possible that with improvements and refinements in the technic of performing the tests, in the preparation of the test solutions, in the interpretation of the character and degree of reactions with standardized high dilutions of different titers on different parts of the body and on previously diseased skin, these tests will ultimately prove their worth in differential diagnosis. While we realize the import of a flare-up of localized lesions following the injection of antigens, we have not had sufficient experience to be able to estimate the significance of such a reaction.

3 One can search for the etiologic agent by microscopic examination for fungi in the affected areas. Fungi may be found in a large proportion of cases of mycosis of the feet, if not on the first search, possibly after repeated efforts. Since the majority of patients have used antiseptic and keratolytic applications on the feet before consulting their physician, they are advised to apply wet dressings of saline solution to the affected parts for several days before a fruitful microscopic search can be undertaken.

In patients presenting simultaneous eruptions on the feet and hands the vesicular lesions of the hands practically always prove to be free from organisms and are therefore manifestations of an allergic state of the skin, clinically and immunologically documented as trichophytids or monilids or perhaps both.

Occasionally a case is met in which fungi can be readily demonstrated in large numbers in dyshidrotic lesions on the hands. These lesions are manifested by primary local ringworm infections of the hand, analogous to those of the feet. Peck⁹ has called attention to the fact that such a primary local dermatophytosis of the hand is capable of producing a dermatophytid of the feet, thus reversing the usual course of events in the sensitized patient.

In the search for fungi from the lesions between and on the toes, and from affected toe-nails, it should be remembered that specimens are best obtained from the peripheral portions of the lesions and that vesic-

9 Peck, S. Epidermophytosis of the Feet and Epidermophytids of the Hands, *Arch Dermat & Syph* 22:40 (July) 1930

ular lesions in the immediate vicinity of the primary process may prove to be sterile and are therefore trichophytids, analogous to those on the hands (Williams¹)

4. Cultural investigations may be carried out. These require an expert mycologist and a good laboratory.

5. By means of biochemical investigations, Marchionini¹⁰ attempted to show that by testing the hydrogen ion concentration of the contents of the vesicles, he was able to distinguish between the true dyshidrosis of Tilbury Fox and the dyshidrosiform eruptions of parasitic or toxic origin. He found that in cases of true dyshidrosis the hydrogen ion concentration of the fluid of the vesicles is 5, the same as that of sweat. In cases of dyshidrosis of mycotic origin the hydrogen ion concentration is 7 (neutral), while in cases of epidermophytids and dyshidrosiform eczema the hydrogen ion is from 7.2 to 8.2 (frankly alkaline). Marchionini admitted that his method is too complicated for every-day routine practice and in lieu of it advocated the use of litmus paper to test the reaction of the fluid of the vesicles. Litmus paper changes color at about hydrogen ion concentration 6.8. In the early stages of true dyshidrosis, the author stated that a definite change from blue to red takes place, owing to retained sweat from the eccrine sweat glands. The contents of the vesicles of infectious dyshidrosis are said to produce an amphoteric reaction, while the contents of vesicles of other dyshidrosiform eruptions, eczema and allergic epidermophytid change red litmus paper to blue. On the strength of these observations Marchionini voiced his opinion emphatically in favor of the conception of true dyshidrosis of Tilbury Fox as a disease *sui generis*.

As McLachlan and Brown aptly stated, these findings call for further investigation and confirmation.⁵

6. Inhibition of growth of fungi, as described by Ayres and Anderson, has already been mentioned. This procedure should be thoroughly investigated.

7. The therapeutic test is helpful. It has been stated by several authors that the secondary "id" eruption clears up when the primary focus of infection is eliminated. Would that that were true! Unfortunately, practical experience has demonstrated that the "id" eruption may, and often does, persist long after all traces of the primary infection have vanished. In this connection, Williams has stressed the necessity of excluding the nails as a potential depot of persistent dissemination of the fungi.

10. Marchionini, A. Pathogenesis and Differential Diagnosis of Dyshidrotic and Dyshidrosiform Diseases of the Hands and Feet, *Dermat. Ztschr.* 58:222 (May) 1930.

With respect to a therapeutic test by means of desensitization, we cannot estimate the value of this method until we have had a great deal more experimental clinical material on which to base definite conclusions. We, as well as a number of other observers, have obtained what appeared to be very good results in selected cases of recalcitrant ringworm and infection with *Monilia*. We believe that with desensitization procedures the future holds in store an efficient and reliable mode of therapy. Perhaps an important phase of the procedure is to make sure that one is using the extract or extracts derived from the actual infecting organism, in contradistinction to the indiscriminate use of "shotgun" vaccines. In all events, the method deserves a thorough and carefully controlled trial. One of the reasons that the reaction to this therapeutic test is difficult of evaluation is that so few patients are willing to submit to inoculations for desensitization without at the same time employing topical remedies of one kind or another. In our opinion, the use of topical remedies, no matter how bland they may be, vitiates the therapeutic test. Furthermore, the eruption is likely to undergo remissions and recurrences, and spontaneous cure may result.

A therapeutic test based on response to roentgen and ultraviolet irradiation and other forms of radiation therapy may have value. With this mode of treatment we have had too few controls to justify an assumption of definite conclusions. We have the impression that response to radiation therapy is at best an uncertain and rather intangible factor in diagnostic differentiation, it will not bear comparison with the therapeutic test of a plaque of mycosis fungoides or a round cell sarcoma, for example, in which roentgen rays are utilized as a test of therapy in the absence of microscopic observations.

SUMMARY AND CONCLUSIONS

- 1 In the United States the majority of vesicular eruptions of the hands in adults, exclusive of occupational eczema, dermatitis venenata and eczema of unknown cause, are accompanied by fungous infections of the feet. Such eruptions on the hands are usually epidermophytids, monilids or trichophytids.

- 2 Owing to the fact that a large proportion of the adult population in this country has, or has had, fungous infection of the feet, positive reactions to the intradermal and patch tests with trichophytin and oidiomycin are of little significance in their direct bearing on the differential diagnosis of a coincident vesicular eruption on the hands.

- 3 The significance of focal, local and general reactions following the intradermal injection of extracts of fungi cannot at present be properly appraised with respect to vesicular dermatoses of the hands and feet.

4 The mere fact that a patient has a vesicular eruption on the hands and a coincident eruption on the feet does not indicate that the eruption on the hands is necessarily or presumably an "id," due to dissemination of fungi or their products (or possibly both) from the original focus on the feet. The eruption on the hands may be caused by a number of demonstrable agents other than fungi, or it may be evoked by a wholly unknown agent.

5 To differentiate these eruptions, a careful history must be obtained from the patient.

6 The diagnosis of "ids" should not be entertained without strongly corroborative evidence, the most important of which is the demonstration of the causative organism, either microscopically or by culture, from the focus of primary infection of the skin or nails.

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II EFFECT OF VARIATION OF RATIOS OF DEXTROSE TO PEPTONE ON COLONIES OF CERTAIN PATHOGENIC FUNGI

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CAMBRIDGE MASS

In a previous paper¹ observations relative to culture mediums for pathogenic fungi, features of importance in the development of a suitable medium and the effects on the morphology of the colony of the variation of the ratio of peptone to dextrose were considered. In this paper, under series 2, a comparison of growths on peptone, proteose peptone or tryptone and dextrose of varying ratio is made, and the importance of physical chemistry in the determination of the morphology of the colony is discussed.

In series 2 the following pathogenic fungi and the two nonpathogenic saprophytes *Lichtheimia* sp. and *Scopulariopsis brevicaulis* were studied: *Achorion Schoenleini*, *Acladium Castellani*, *Candida candida*, *Endodermophyton tropicale*, *Endomyces capsulatus*, *Endomyces dermatitidis*, *Epidermophyton cruris*, *Epidermophyton inguinale*, *Geotrichum Bachmann*, *Glenospora Gammeli*, *Indiella americana*, *Microsporon Audouini*, *Microsporon felineum*, *Microsporon gypseum*, *Monosporium apiospermum*, *Monilia albicans*, *Oospora humi*, *Sporotrichum Schenckii*, *Trichophyton crateriforme*, *Trichophyton granulosum*, *Trichophyton gypseum-asteroides*, *Trichophyton gypseum-lacticolor*, *Trichophyton interdigitale*, *Trichophyton japonicum*, *Trichophyton niveum*, *Trichophyton sulfureum* and *Willia anomala*.

SERIES 2

A comparative study was made of growths on peptone, tryptone and proteose peptone in an effort to decide which medium is superior. The same abbreviations are used as were used in the former paper,¹ together with T indicating tryptone and P indicating proteose peptone. The following mediums were used: S, W, L and R (1, 4, 8 and 12

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1 Williams, J W. I. Effect of Variation of Ratios of Dextrose to Peptone on Colonies of Certain Pathogenic Fungi, *Arch Dermat & Syph* 32:893 (Dec) 1935

per cent peptone, respectively), ST, WT, LT and RT (1, 4, 8 and 12 per cent tryptone, respectively), SP, WP, LP and RP (1, 4, 8 and 12 per cent proteose peptone, respectively, to which was added 4 per cent dextrose), ST1, WT1, LT1 and RT1 (1, 4, 8 and 12 per cent tryptone, respectively, to which was added 1 per cent dextrose), ST4, WT4, LT4 and RT4 (1, 4, 8 and 12 per cent tryptone, respectively, to which was added 4 per cent dextrose), SP1, WP1, LP1 and RP1 (1, 4, 8 and 12 per cent proteose peptone, respectively, to which was added 1 per cent dextrose), and SP1, WP4, LP4 and RP4 (1, 4, 8 and 12 per cent proteose peptone, respectively, to which was added 4 per cent dextrose) By peptones is meant peptone, proteose peptone and tryptone

Difficulty was encountered with the higher concentrations of proteose peptone because of the failure of the mediums to solidify Therefore, observations on RP1, RP4 and LP4 are often omitted Another difficulty with this medium was the depth of color, which was often imparted to the growth and which obscured any organismal pigment that might be present

For convenience the groupings used in series 1 are followed in this paper

GROUP A

Achorion Schoenleini—As the concentration of peptone, tryptone or proteose peptone is increased, the growth becomes more radiate, cratered and irregular As the concentration reaches 8 and 12 per cent, the growth begins to appear wet in certain areas The growth is slightly greater on 8 and 12 per cent concentrations than on 4 per cent concentration and are considerably greater than on 1 per cent concentration It is probable that the best growth is that on 4 per cent tryptone, and the next best growth is on 8 and 12 per cent proteose peptone and 8 per cent peptone

When 1 per cent dextrose is added to the peptones, the culture on ST1 shows a dainty growth with twenty radii centrally, while the center of the growth on WT1 shows cracking and the edges are heaped up On SP1 there are irregular radii and cratering centrally, with cracking, giving a granular appearance On WP1 the central cracking is coarser and the edges are more heaped up than on ST1, WT1 and SP1 On W1 the growth is larger, and there is more white powder and the growth is more irregular centrally than that on P1 The growths on the peptones in higher concentrations seem to show more aerial mycelium and become, although more irregular, more pleomorphic The growths on tryptone and proteose peptone seem to be best differentiated On SP1 and ST1 there is a suggestion of pink

When 4 per cent dextrose is added to the peptones, the growths on S4 and ST4 show some buff color and powder and are better differentiated than those on other mediums With a higher concentration of peptone the growths either are too wrinkled or acquire aerial mycelium and become pleomorphic On the peptones in higher concentration than 1 per cent and on 4 per cent peptone the differentiation of the growths is 3+ Tryptone causes the best differentiation of the growth

Epidermophyton Cunicus.—A fawn-colored powder is more apparent on peptone and proteose peptone than on other mediums. The growths on the 8 per cent concentrations of each of the peptones show more marked cratering, more powder and a more heaped-up edge than those on other concentrations. The growth on WR shows as pronounced change as that on LT or L. The growth is small until the concentration of peptone reaches 8 per cent, except on the 4 per cent proteose peptone.

When 1 per cent dextrose is added to the peptones, the growth on W1 reveals an amber-colored base and a brownish-yellow tinted powder on some plants and is slightly cratered with a few radii. On P and R the changes on the addition of 1 per cent dextrose are less regular than those on W1, but they are marked. There is a tendency for the powder to be light pink on L1.

When 4 per cent dextrose is added to the peptones, there is more pleomorphism, especially on 1 per cent peptone. The growths on the other concentrations are not especially characteristic. Pleomorphism seems to decrease with an increase in the concentration of peptone. Powder varying from yellow to lemon is present, especially on WT4 and WP4.

Indiella Americana.—The growth on S4 is light olive-green, radiate and of doeskin variety and is by far the most typical. With an increase in the concentrations of peptone there is a tendency to frosting, nodular appearance, spicules and pleomorphism. As on S4, the growth on SP4 is light olive-tan, but it does not show the regularity of that on S4. On S1 the growth is white but shows good differentiation. The growths on RP1 and RT1 look like fur on a teddy-bear. The growth on W4 shows a wrinkled cream-puff appearance centrally. The extent of the growth seems to increase with the concentration of peptone and dextrose.

Microsporon Felinum.—The growths on the peptones in various concentrations are fawn-colored. On 1 per cent peptone the growth is somewhat scant, but on higher concentrations the growths take on the appearance of doeskin. On 8 and 12 per cent concentrations of the peptones the growths are more radiate and less pleomorphic than those on mediums of lower concentration.

On the addition of 1 per cent dextrose, the growth on W1 shows some of the appearance of doeskin, is wrinkled and has many radii. The growth on W1 and that on RT1 are very good, the latter has a brownish color. The growths have a color varying from yellow to cream.

On the addition of 4 per cent dextrose, the growth on R12 has a skinlike appearance and shows better differentiation. In these observations the ratio of dextrose to sugar seems important. The growth is yellowish and cream-colored. The best differentiation is found in the growths on the peptones. There is more growth on proteose peptone. Pleomorphism decreases with an increase in the concentration of peptone and a decrease in the concentration of sugar.

Monosporium Apiospermum.—Only the growths on peptones in a concentration of 1 per cent show the typical white mycelium (thin film). On W and WT there are radii. As the concentrations of peptones are increased, there is an increase in frosting, in the granular and glassy appearance, in the spicule-like mycelium and in waxiness. On R the glassy, beeswax growth appears as though meshed, or mitered together. On the addition of 1 per cent dextrose, there appears a white film of mycelium, which becomes scant and the growth is heaped up and wrinkled. When the concentration of the peptones is increased over 1 per cent the previously described characteristics usually give way to a granular frosted

surface, waxiness and stubble mycelium, these being superseded, with an increase in concentration, by a waxy surface. There are black areas at the base.

On the addition of 4 per cent dextrose, there is more white mycelium, but this gives way to waxy and frosted areas (even on 1 per cent proteose peptone) with an increase in the concentration of the peptones. Generally, the growth of this organism seems to increase with an increase in the concentration of the peptone and dextrose (except on 4 per cent dextrose and tryptone, where it decreases), and waxiness increases with an increase in the concentration of the peptones, especially on proteose peptone. A decrease in the concentration of dextrose is also important. Blackening of the base is apparent on 1 per cent concentrations of the peptone.

Trichophyton Crateriforme—Growths of this organism are comparatively good on all mediums. They are too wrinkled when the concentration of peptone is 8 or 12 per cent and when dextrose is not added to the 1 per cent concentrations. The growths on peptone and tryptone are superior to those on proteose peptone. There is no growth on RT4.

Trichophyton Granulosum—On 1 per cent concentrations of the peptones the growths are mycelial. On 4 per cent and higher concentrations of the peptones there is a tendency for a portion of the growth to become bare of mycelium and even to appear waxy, so that on 12 per cent proteose peptone and 12 per cent tryptone peptone the growth becomes like a collapsed, crinkled cream puff, giving the appearance of the endodermophytons on W1.

When 1 per cent dextrose is added to the various concentrations of the peptones, the white mycelium becomes slightly diminished with an increase in the concentration. On L1 and R1 there are concentric rings in the growth, while on W1 the rings are suggested. An increase in the concentration of proteose peptone causes a tendency for the growth to become bare of mycelium, to produce more powder and to become more wrinkled. This effect is seen to a greater extent on an increase in the concentration of tryptone.

As the concentration of the peptones is increased and that of dextrose is decreased, the growths tend to lose their aerial mycelium.

When 4 per cent dextrose is added to the medium, the growth becomes successively less pleomorphic and shows wrinkling, radii and powder. With an increase in the concentration of the peptones the growths become less mycelial on all mediums.

As the concentration of the peptones is increased and that of dextrose is decreased, the growths tend to lose their aerial mycelium and become more wrinkled and radiate, on RT1 they even become granular.

Trichophyton Gypseum-Asteroides—The growths on the 1 per cent concentrations of the peptones are mycelial. Except on proteose peptone, on which the growths are irregular, the growths on the remaining concentrations show cratering, wrinkling and powderiness. The growths on W, L and WT are probably most typical.

When 1 per cent dextrose is added to 1 per cent concentrations, the growths are mycelial. With an increase in the concentration of peptone the growths become successively less mycelial, that on W1 showing more cratering and that on L1 much less mycelium. The growths on proteose peptone are irregular. The growth on WT1 shows cratering, with radii, and those on LT1 and RT1 show less mycelium and a more wrinkled and radiate effect.

When 4 per cent dextrose is added to peptones of 4 per cent or higher concentration, there are powderiness and an increasing tendency to cratering and

wrinkles, there is a marked decrease in the growth on LT4, and there is no growth on RT4. There is a faint orange powder on L4.

Trichophyton Gypseum-Lacticolor—As the concentration of peptone is increased, there is a tendency to an increase of powder, cratering, wrinkling and radii. The growths on 8 and 12 per cent concentrations of the peptones show the greatest differentiation.

On the addition of 1 per cent dextrose, the growths, although slightly cratered on the 1 per cent concentrations of the peptones, become more cratered, less mycelial and more powdery. Mediums of 8 and 12 per cent concentration of the peptones seem the more suitable.

On the addition of 4 per cent dextrose, the growths on 1 per cent concentrations of the peptones show marked mycelial development, the growths become cratered, powdery and wrinkled with an increase in the concentration of peptone. There is an orange tint on R4.

Trichophyton Interdigitale—On the various peptones there is more marked differentiation with an increase in the concentration. The development of the growths on mediums of the next higher concentration of proteose peptone and tryptone seems to correspond more closely with that of the growth on peptone. A concentric band with a few radii appears on L, and cratering and some powder are noted on R.

On the addition of 1 per cent dextrose and with an increase in the concentration of the peptones over 1 per cent, the aerial mycelium is gradually lost and the growths become powdery, showing wrinkling, cratering and a brownish tint.

On the addition of 4 per cent dextrose, there is a great increase in aerial mycelium on the 1 per cent concentrations of the peptones, which becomes less with an increase in the concentration, with knobbing, cupping, at times radii and a cream-colored tint, except on tryptone, on which there is a pink tint.

An increase in the concentration of peptone and a decrease in that of dextrose causes a decrease of mycelium and an increase of powderiness, radii and wrinkling.

Trichophyton Niveum—On RT there is a platter-like growth with an amber-colored edge. On the peptones in 1 per cent concentrations, the growths are pleomorphic, becoming less pleomorphic as the concentration of peptone is increased and showing powder, frosting at the edge, wrinkling and cratering.

On the addition of 1 per cent dextrose, some cratering becomes apparent on 1 per cent peptones, but the cratering increases together with radii and irregularity, with an increase in the concentration of peptone.

On the addition of 4 per cent dextrose, there is a suggestion of pink on SP4, on 1 per cent peptones there is considerable pleomorphism, which decreases with an increase in the concentration and is accompanied by cratering, wrinkling and radii. On RT there is no growth. The growths seem to increase in amount with an increase in the concentration of sugar.

Trichophyton Sulfurcum—The mycelium is irregular. On R there is a powdery and slightly cratered growth, with a creamy tint, that on RP is somewhat similar. The growths on these mediums are better differentiated. The growths on tryptone seem to have more mycelium than those on LT being better developed.

On the addition of 1 per cent dextrose, the mycelium seems to increase with an increase in the concentration of peptone. It is probable that the better mediums are those of 1 per cent concentration of the peptones.

On the addition of 4 per cent dextrose, the 1 and 4 per cent concentrations of the peptones are probably the best mediums.

Development and pleomorphism seem to increase with an increase in the concentration of peptone and sugar. The growths at least suggest the sulfur tint, which varies.

GROUP B

Epidermophyton Inguinale—W and WP are the best mediums, with powder from fawn to light yellow, and with cratering and radii. On R there is a tint of pink. High concentrations cause too much wrinkling, and pleomorphism occurs on proteose peptone.

On the addition of 1 per cent dextrose, the growths on 4 per cent concentrations of the peptones show the better differentiation, but the differentiation is also good on the 1 per cent concentrations. Changes are more marked on proteose peptone than on other mediums. Amber and yellow pigment are noted.

On the addition of 4 per cent dextrose, the growths become more pleomorphic and more wrinkled as the concentration of peptone is increased, with the exception of those on proteose peptone, on which pleomorphism apparently decreases slightly. There is amber pigment.

Microsporon Audouinii—The growths on 4 and 8 per cent tryptone are probably the best differentiated, with faint orange radii and slight sinking of the plant centrally, the growth on 4 per cent peptone is next best. On the addition of 1 per cent dextrose the growths on peptone are better, those on L1 being best and those on LT1 and LP1 next best. All show coloration from light orange to tan. An increase in the concentration of peptone to R1 seems to increase the mycelium, while a decrease in the concentration from 8 per cent results in somewhat less differentiation.

On the addition of 4 per cent dextrose to 1 per cent peptone, a beautiful orange-colored growth results, with low mycelium, as the concentration of peptone is increased, there are apparently more powder and wrinkling. The growths on proteose peptone and tryptone are more mycelial than those on the aforementioned mediums, and there are no growths on the 4, 8 and 12 per cent tryptone.

Microsporon Gypseum—On the peptones the pigmentation ranges from tan to salmon, on 4 per cent peptone, 4 per cent proteose peptone and 8 per cent tryptone there seems to be better differentiation of the growths, with well defined radii, wrinkling and comparative freedom from aerial mycelium.

On the addition of 1 per cent dextrose, the growths on 4 and 8 per cent concentrations of the peptones show up well, with a powder from orange to tan and radii toward the center, with some wrinkling.

On the addition of 4 per cent dextrose, there is more mycelium, which is reduced by an increase in the concentration of the peptone, but not sufficiently to make the growth as typical as those previously described.

Trichophyton Japonicum—There are not many growths on the peptones without dextrose. There is more pigment on 4 per cent peptone and 4, 8 and 12 per cent tryptone and less pigment on proteose peptone.

On the addition of 1 per cent dextrose there is more growth, a yellow tint being apparent on the growth on 1 per cent peptone, with little discoloration of the medium, on an increase in the concentration of peptone the browning of the medium becomes more intense. On proteose peptone there is less browning and slightly less growth.

On the addition of 4 per cent dextrose there is more pigment, especially on 4 per cent peptone, with the growths on other concentrations showing less pig-

ment, wrinkling and cratering become marked in growths on higher concentrations of the peptones, especially of proteose peptone. The extent of the growth is increased on all mediums.

GROUP C

Endomyces Capsulatus—The thin mycelium decreases with an increase in the concentration of peptone, and its place is taken by a coarser mycelium and progressively more frosting of fawn color. The growths are more profuse on proteose peptone and tryptone than on peptone, on proteose peptone in high concentrations the mycelium is especially matted, and on tryptone there appears a nipple-like base from which spicules extend, often covered with bits of white mycelium or attached to the adjacent glass by footlets.

With 1 per cent dextrose a somewhat similar appearance occurs with an increase in the concentration of peptone. On 1 per cent concentrations of the peptones the growths are white and mycelial, except on proteose peptone, where the growths correspond more to that on 4 per cent peptone. On all mediums with 1 per cent dextrose the growths are more profuse and assume the appearance of beeswax.

With 4 per cent dextrose the growth on 1 per cent peptone has a light fawn-colored mycelium at the center, with frosting around it, this formation is exaggerated, the mycelium becomes coarser and more matted and the frosting is greater as the concentration of peptone is increased. On 1 per cent proteose peptone there is white mycelium, but the extent of the growth quickly decreases as the concentration of proteose peptone is increased. There is no growth on RPI. On tryptone and peptone the growths seem to increase with an increase in the concentration of dextrose and tryptone or peptone.

Endomyces Dermatidis—On 1 per cent peptone there is an area of white mycelium centrally. On an increase in the concentration of peptone the mycelium becomes matted and spicules appear. The appearance is similar on tryptone, but the formations seem more advanced on proteose peptone and show some wrinkling and radii on an increase in the concentration. There is frosting on all mediums.

With 1 per cent dextrose the growth on 1 per cent peptone is waxy, light gray and smooth except for an occasional speckling of white mycelium. On 4 per cent peptone the growth shows more aerial mycelium, but the mycelium becomes more matted as the concentration of peptone is further increased. On 1 per cent proteose peptone the growth shows the white mycelial duvet, those on the higher concentrations showing mycelial spicules and frosting. On 1 per cent tryptone the growth shows a pleomorphic white mycelium which becomes matted and shows spicules as the concentration of tryptone is increased, the mycelium, even on the 1 per cent concentration, has a fawn tint. The extent of the growth on tryptone is increased over that on the aforementioned mediums. With 4 per cent dextrose the growth on 1 per cent peptone is smooth and waxy, with rare, waxy mycelium heaped radially to the plant, the mycelium becomes matted on 4 per cent peptone and tends to become more profuse with a further increase in the concentration of peptone. There is not as extensive a growth with 4 per cent dextrose as with 1 per cent dextrose. On 1 per cent proteose peptone the growth is white and mycelial, but it becomes waxy with an increase in the concentration. The growths on 1 and 4 per cent tryptone are pleomorphic, and no growth occurs on 8 and 12 per cent tryptone. This is the only instance in which growth does not seem to increase with an increase of the concentration of dextrose and peptone.

Glenospora Gammeli—On 1 per cent peptone there is a layer of white mycelium, as the concentration of peptone is increased, coarser mycelium, spicules and addi-

tional frosting become apparent, together with bits of white mycelium here and there. The growths on proteose peptone and tryptone are similar.

With 1 per cent dextrose the growth on 1 per cent peptone shows a white mycelium, with an area cratered centrally and slightly powdery, through which shows a frosted surface below. The mycelium becomes more matted and spicule-like as the concentration of peptone is increased. On proteose peptone the growth seems further advanced, and on 12 per cent peptone there seems to be a tendency for the spicules to become more sparse and finer than on other concentrations. The growths decrease on 8 and 12 per cent tryptone and become smoother, otherwise they resemble those on peptone.

With 4 per cent dextrose the mycelium is less evident, and the growth is more wrinkled and more uniformly powdered, with frosting at the edge, on 1 per cent peptone with 4 per cent dextrose than with a reduced concentration of dextrose. As the concentration of peptone is increased, the growth shows more aerial mycelium. On 1 per cent proteose peptone the growth is waxy, but it shows aerial mycelium with an increase in the concentration. Tryptone acts as peptone, causing the growth to produce feelers which attach themselves to the glass on the 4 per cent concentration, there is a hardly appreciable growth on 8 and 12 per cent tryptone.

The growth seems to increase with an increase in the concentration of peptone and dextrose, except probably in the case of tryptone. When the mycelium disappears a fawn color is assumed. The growths on 1 per cent peptone and 1 per cent proteose peptone show more cratering and wrinkling than those on the other mediums.

GROUP D

Endodermophytonropicale—The growths on 1 per cent concentrations of the peptones seem somewhat powdery, on mediums of higher concentration the growths become wrinkled and heaped up, on 8 and 12 per cent proteose peptone the growths resemble wrinkled cream-puffs, their coarseness increasing with the concentration of the peptone.

With 1 per cent dextrose there is more growth, wrinkling increasing with an increase in the concentration of the peptone. The growth tends to increase on 1 per cent proteose peptone.

With 4 per cent dextrose the growths are darker and slightly more profuse, but on tryptone they decrease with an increase in the concentration, until there is no growth on 12 per cent tryptone.

I have considered the collapsed cream-puff appearance typical for most of these growths.

GROUP F

Acladium Castellani—On 1 per cent peptone there is a small, shell-like growth, with faint radii and a concentric rim, it is fawn-colored and slightly raised. With an increase in the concentration the growths become black, they are finely radiate on the 4 per cent concentration and more coarse on 8 and 12 per cent concentrations, the growths become lighter at the borders as the concentration increases. On 1 per cent proteose peptone the growth is petal-like, being raised at the center, where there is a sparse white mycelium. The growths on all the mediums darken, but on 4 per cent proteose peptone the growth is black, irregularly heaped up and radiate, with a serrated edge while on 8 and 12 per cent proteose peptone the growths are more a fawn color. On 1 per cent tryptone the growth is black, but it becomes lighter as the concentration of tryptone is increased, that on 4

per cent tryptone being black, but those on 8 and 12 per cent tryptone being fawn-colored

With 1 per cent dextrose the growth increases and is darkened. On 1 per cent peptone the growth is a light fawn color, becoming dark toward the center of the colony, with fairly deep radii, the growth on 4 per cent peptone is the darkest, those on 8 per cent and on 12 per cent peptone being more fawn-colored. With an increase in the concentration of peptone there seems to be a slightly greater increase in wrinkling. On proteose peptone the growth seems to be more waxy and heaped up with an increase in the concentration and is fawn color. On 1 per cent tryptone there are well formed, multiple concentric rings, with radial folds, and the color is dark brown, with an increase in the concentration the rings become less pronounced and a granular appearance develops.

With 4 per cent dextrose the medium is darkened and there is probably an exaggerated growth, with more heaping, wrinkling and mycelial stubble centrally with an increase in the concentration of the peptones.

The growth apparently increases with an increase in the concentration of the peptone and sugar.

Candida Candida—On the peptones with an increase in the concentration the growths become coarse, wet and wrinkled, there is a subsurface mycelium which decreases with an increase in the concentration. On proteose peptone the growth is slightly less than that on peptone but is more heaped up and radiate, and the subsurface mycelium is sparse. On tryptone the growth is more profuse than that on peptone, there is less subsurface mycelium and it decreases with an increase in the concentration. There are a few white granules on 8 and 12 per cent proteose peptone and some radii on 12 per cent proteose peptone.

With 1 per cent dextrose the growths are more profuse and latticed on 1 and 4 per cent peptone than on the aforementioned mediums, the growth is wetter on 4 per cent peptone and shows a little fine stubble mycelium, development is radiate from the points of inoculation. There is stubble mycelium on 8 per cent peptone, on 12 per cent the growth is more blotchy. On mediums of more than 4 per cent concentration there seems to be a decrease in subsurface mycelium with an increase in the concentration. On proteose peptone there are more profuse growths than on peptone, and subsurface mycelium decreases with an increase in the concentration. The growth is more moist on tryptone than on the aforementioned mediums, and on 8 and 12 per cent tryptone the growth appears to be sprinkled with coarse particles.

With 4 per cent dextrose the growth on 1 per cent peptone shows a smooth, waxy and radiate growth, with a slightly heaped-up central area, the growth increases as the concentration of peptone is increased and becomes more irregular and heaped, stubble mycelium appears, a narrow edge is radiate, but the rest of the growth is corrugated. The growths on all mediums are moderately wet, and there is less subsurface mycelium with an increase in the concentration of peptone. The growth is much heaped up and irregular on proteose peptone. On 1 per cent tryptone the growth is smoothly radiate from a somewhat granular center, the granular center becomes larger with an increase in the concentration of tryptone until it is the color of brown sandpaper on 12 per cent tryptone. The growth decreases with an increase in the concentration of tryptone.

The subsurface mycelium decreases with an increase in the concentration of peptone and probably with an increase in the concentration of dextrose; the mycelium is least evident on proteose peptone.

Monilia Albicans.—On 1 per cent peptone there is little else than subsurface mycelium, which decreases with an increase in the concentration of peptone. On 4 per cent peptone the growth shows radii, on 8 per cent peptone, a latticed center and on 12 per cent peptone a heaped-up and somewhat radiate formation. On proteose peptone the growths are less uniform, wetter and more granular and show very little subsurface mycelium. On 1 per cent tryptone there is more subsurface mycelium, on 4 per cent tryptone the growth becomes more uniform and radiate, with a latticed center. The growths become less latticed, wetter and more granular as the concentration of tryptone is further increased. The growths increase with an increase in the concentration of the peptones.

With 1 per cent dextrose and peptone a latticed center appears which becomes finer and more heaped up as the concentration is increased, the growth is more radiate on 1 per cent peptone, those on the higher concentrations being more latticed and more radiate. On proteose peptone the growths are wetter and not as finely latticed as on the aforementioned mediums, on 4 and 8 per cent proteose peptone the growths give a mucoid effect, and on 1 and 12 per cent proteose peptone, a coarse, latticed effect. On 1 per cent tryptone the growth has a latticed, honeycomb center, the growth on 4 per cent tryptone is more uniformly latticed, the growth on 8 per cent tryptone is more heaped up and the growth on 12 per cent tryptone is more granular.

With 4 per cent dextrose the growth on 1 per cent peptone has a honeycombed center, which is radiate and heaped up, there is less lattice effect on 4 per cent peptone, but the edge of the growth on this concentration and almost all of the 8 per cent peptone, are coarsely granular, with radii at the edge, the growth on 12 per cent peptone is very much latticed throughout. The growth is not uniform on proteose peptone. The growths are coarsely granular on 4 and 8 per cent tryptone, leaflike on 1 per cent tryptone and somewhat liquid on 12 per cent tryptone.

Generally, there is greater growth with an increase in the concentration of peptone and dextrose.

Sporotrichum Schenckii.—On 1 per cent peptone there are a powdery surface like whitewash and subsurface mycelium, of which there is less as the concentration of peptone is increased. On 4 per cent peptone there is a purposeless growth, and on 8 and 12 per cent peptone the growths are increasingly more irregularly radiate. On 1 per cent proteose peptone there are a suggestion of radii and a white powdery appearance at the edge of the growth, with the increase in concentration the growth becomes wet and mucoid. On 1 per cent tryptone frostiness and subsurface mycelium appear, which decrease with an increase in the concentration. White granules appear on 8 and 12 per cent tryptone. The extent of the growth increases in this group and with an increase in the concentration there is an increase in radii.

With 1 per cent dextrose the growth on peptone is increased, on 1 per cent peptone the growth is spattered with large grains of powder resembling whitewash and a little subsurface mycelium. The growth on mediums of higher concentration are waxy, with radii and a brushlike mycelium at the periphery. On 1 per cent proteose peptone there appears white powderiness like down, with radii giving the appearance of wrinkled doeskin, there is a scant subsurface mycelium, and isolated colonies give a starlike effect with their radii. On mediums of a higher concentration the growths are more mucoid and wetter. On 1 per cent tryptone the growth is radiate but not powdery, on other concentrations of tryptone the growths are similar to those on peptone.

With 4 per cent dextrose the growth on 1 per cent peptone is lattice-like and radiate, with a smooth formation on the surface at the periphery. On 4 per cent peptone the growth is like a shield spattered with coarse sand (mycelial stubble), on 8 per cent peptone the growth becomes irregularly radiate and heaped up. On 12 and 8 per cent peptone the growth increases and is wetter. On 1 per cent proteose peptone the mycelium is sparse like sprigs and there is a waxy granular appearance, on higher concentrations the growths become wetter. On 1 per cent tryptone there is a dry granular growth, on 4 per cent tryptone the growth is finely radiate, and on an increase in concentration the growths are coarsely granular, with nests of radii.

An increase in the concentration of sugar and peptone results in an increased growth.

GROUP G

Geotrichum Bachmanni.—On peptone the growth increases with an increase in the concentration. There are slightly more extensive growths on proteose peptone and tryptone than on peptone. On 12 per cent tryptone there are white granules.

With 1 per cent dextrose the growth increases, becoming more blotchy. The growths are blotchy on the proteose peptone, that on 1 per cent proteose peptone is smoother and more radiate. On 1 per cent tryptone there is a tendency to heaping, with radii, on other concentrations granules are noted.

With 4 per cent dextrose the growth on 1 per cent peptone is smooth, with a suggestion of a concentric ring, the rest is blotchy but is increased in thickness over the growth on 1 per cent dextrose. On proteose peptone the growths are smoother but have an irregular surface. On 1 per cent tryptone the growth is more frosted and puckery, on 4 per cent tryptone there is an irregular ribbed appearance, with a scant, white fuzz over the surface, on 8 and 12 per cent tryptone granules are noted.

Lichtheimia sp.—As the concentration of peptone increases, the aerial growths become successively diminished, until on 8 and 12 per cent peptone a frosted, waxy surface with a border showing scant low mycelia appears. On 4 per cent peptone mycelium is much reduced, low and matted to the surface. The growths on proteose peptone are similar, but a reaction to an increase in the concentration of peptone occurs sooner, and the growths are thicker and become granular. On tryptone the growths are similar to those on peptone, but changes begin on a slightly lower concentration.

With 1 per cent dextrose there is more mycelium and the growth is more extensive, on 4, 8 and 12 per cent peptone, successively, the mycelium fills less of the tube and the growths become frosted. This occurs on tryptone and proteose peptone.

With 4 per cent dextrose the mycelium becomes more profuse and fills less of the diameter, on 8 and 12 per cent peptone the growths are more drawn. On 8 and 12 per cent proteose peptone the growths are like beeswax. Aerial mycelium is noted in all the tubes of tryptone.

Aerial mycelium increases with an increase in the concentration of dextrose and decreases with an increase in the concentration of peptone, but the effect of peptone is largely offset when 4 per cent dextrose is used with peptone and tryptone.

Oospora Humi.—There is a low, short, velvety mycelium on peptone, on 12 per cent peptone there are fewer than on the other concentrations, otherwise the surface is frosted and the growth increases with an increase in the concentration of peptone. The growths on proteose peptone are similar to those on peptone but

with less mycelium. On tryptone of more than 1 per cent concentration the growths have a ribbed and granular appearance, and white mycelium is largely absent from the growths on 4 and 12 per cent tryptone. The growths are more profuse on tryptone than those on peptone.

With 1 per cent dextrose the growths are more extensive, of somewhat ribbed appearance. On 1 per cent proteose peptone the growth is more profuse and ribbed radially. Growth on tryptone are more blotchy.

With 4 per cent dextrose the growth on 1 per cent peptone develop a white mycelial layer, giving a powdery appearance, with an increase in the concentration the growths become thicker and more like beeswax, with an appearance of sand-paper on 12 per cent peptone. The growths are more profuse on proteose peptone and tryptone than on peptone.

Scopulariopsis Brevicaulis—As the concentration of peptone is increased the growths become more wrinkled, lighter brown, wetter and more finely granular and there is an increase in aerial mycelium. There is a tint of green on 12 per cent peptone. There is more interlocked wrinkling on proteose peptone, with more growth, more wrinkling and more uniformity of appearance. On tryptone the growths are more wrinkled than those on peptone, and on 8 and 12 per cent tryptone the growth is almost entirely wet.

With 1 per cent dextrose the growth on peptone shows less wetting, the color is not lost as quickly with an increase in the concentration of the peptone, but heaping up and a tendency to radii are more marked, and there is probably slightly more aerial mycelium. On proteose peptone the growth is wrinkled at the center, with white granules on the 1 per cent concentration. On 1 per cent tryptone there is a verrucoid appearance at the center, on 8 and 12 per cent tryptone the growths are partly wet. The mycelium is matted at the center of the growth on 8 per cent tryptone, and fine, long, hairlike ends of mycelium are seen at the center of the growth on 12 per cent tryptone.

With 4 per cent dextrose the color on 1 per cent peptone is diminished, more wetting is noted on 8 per cent peptone, and there are areas of white mycelium. The growths become lighter as the concentration of peptone is increased. The growths are much wrinkled on proteose peptone and become lighter in color as the concentration of peptone is increased. On 1 per cent tryptone the growth shows a verrucoid appearance and is cream-color, it is heaped up and somewhat concentric and has a scattering of fine white powder. The growth on 4 per cent tryptone is fine, like verruca, with a brown powdery surface, the growths on 8 and 12 per cent tryptone are wet and very wrinkled, with practically no mycelium, and are a lighter brown than that on 4 per cent tryptone.

The growths seem to increase with an increase in the concentration of peptone and sugar.

Willha Anomala—On peptone the growths increase with the increase in the concentration. The edge is irregularly serrated on 1 per cent peptone, the growths seem lumpy on mediums in higher concentrations. The colonies are more blotchy on proteose peptone and the growths are more profuse than those on peptone. On tryptone the growths are similar to those on peptone.

With 1 per cent dextrose the growths increase with an increase in the concentration of the peptones, especially of proteose peptone.

With 4 per cent dextrose, the growth on 1 per cent peptone shows radiate surface mycelium at the border and into the medium (the development of mycelium is slight on 1 per cent peptone with 1 per cent dextrose), the growth is more pro-

fuse than that with 1 per cent dextrose. The growths on proteose peptone are smeary. On tryptone the growths resemble those on peptone but are drier, with a sandpaperiness, slightly fuzzy surface and a suggestion of radii.

GENERAL OBSERVATIONS

In a perusal of the literature I have found little reference to the use of tryptone and proteose peptone for the growth of pathogenic fungi. Leonian² used proteose peptone to a limited extent. Because of the specialized use of tryptone and proteose peptone in the cultivation of micro-organisms and because of their variation in composition,³ it seemed fitting to use them in the effort to find a better medium for the cultivation of pathogenic fungi. The mediums were prepared in the same way as those of peptone used in the series reported previously,¹ and the organisms were grown under similar conditions.

The results on the several mediums differed in numerous respects. In general, with like concentrations of the three peptones there seemed to be more advanced changes on proteose peptone and least advanced changes on tryptone. Often with 8 and 12 per cent proteose peptone and 4 per cent dextrose and with 12 per cent proteose peptone and 1 per cent dextrose solidification with 1.5 per cent agar did not take place, in which case the tubes were discarded. With 4 per cent dextrose and 8 and 12 per cent tryptone, diminished or no growth occurred in several instances, indicating a factor interfering with the growth of the organisms.

A change most frequently noted on proteose peptone and less often noted on tryptone was iridescence of the surface of the medium about the plant. Since this occurred frequently, I believe that it was probably not sufficiently characteristic or fundamental to be of value in differentiation.

In general, on all mediums the growths increased with an increase in the concentration of the peptones and dextrose. In most instances pleomorphism increased with an increase in the concentration of dextrose but decreased with an increase in the concentration of peptones.

There were a few instances in which a constant percentage of dextrose and an increase in the concentration of peptone seemed to result in increased pleomorphism. It is possible that the ratio of these two ingredients was determinant. With an increase in the concentration of peptone there was an increase in wrinkling, cratering, wetness, frosting, waxiness and coarseness of the mycelium (stubble mycelium, etc.), especially on mediums in which dextrose was present. There

² Leonian, L. H. Effect of Position of Inoculum on Growth of Some Trichophytons in the Presence of Dyes, *Arch. Dermat. & Syph.* 25:1016 (June) 1932.

³ Manual of Dehydrated Culture Media and Reagents, ed. 4, Detroit, Difco Laboratories, 1933.

were some indications that waxiness occurred in the stage following wetness of the mycelium on an increase in the concentration of peptone. In a few growths subsurface mycelium was marked, this was present especially in the growths on 1 per cent peptone and decreased with an increase in the concentration of peptone.

In general the growth on the several peptones was somewhat similar. I have not attempted to list in detail the variations in color, for, as stated previously, this would be difficult because of changes in color resulting in many of the mediums from an increase in the concentration. An attempt has been made in the accompanying table

The Differentiation of Various Organisms According to the Medium Employed

	Peptone		Proteose Peptone		Tryptone	
	M*	D	M	D	M	D
Achorion Schoenleinii	R, W1, L1 W4	2½ 3	R, S1, W1	3	R, W1 S1	3 3½
Epidermophyton cruris	L, W1, L1	3	WP, W1, LT1 WP1, LP	3 3½	LT, LT1	3
Epidermophyton inguinale	R, W4, W1, S4	1½ 2	WP LP	2 2½	WT1, RT1 LT1	1½ 1½
Indiella americana	S1 S4	2½ 3½	SP4	2½	ST1	2½
Microsporon Audouinii	L1 W1	3 2	WP1	2	WT, ST1 WT1, LT1	2 2
Microsporon felineum	R, L1, R4 W1, S1	1 1½	L, R, L1 R1	1 1½	LT R, L, L1	2 1
Microsporon gypsum	L1 W1	2½ 3½	LP1 WP1	4 3	LT1 WT1	3½ 3
Trichophyton crateriforme	L W1, L1	3 2½	LP SP1	3 3½	RT ST1	2½ 3½
Trichophyton granulosum	R	2	RP	1½	RT, RT1	2½
Trichophyton gypsum asteroides	R, R1	1½	WP1 LP1	2½ 3	RP, WT LT1	2½ 2½
Trichophyton gypsum lacticolor	W1 R, R1	½ 2½	LP, WP LP1, RP1 WP4, LP4	2 2½ 2½	WT, LT1 LT, WT1	2½ 2
Trichophyton interdigitale	R, R1, R4 L1	1½ 1½	RP1, RP4	1½	RT1, RT4	1½
Trichophyton niveum	L, W1	2½	LP, WP1	2½	RT LT, WT1	3½ 2½
Trichophyton sulfureum	S4 W4	2½ 3	RP, SP1	2	RT1	2

* Under M is indicated the medium and under D the differentiation

to indicate mediums giving good differentiation. The judgment as to differentiation may be questioned. The suggestions with reference to increasing the differentiation are along the line of reducing aerial mycelium. For such a reduction, with some organisms a high concentration of peptone was necessary. In fact, variation with regard to the reduction of aerial mycelium by means of an increase in the concentration of peptone occurred to a considerable degree with different organisms. To determine whether this method is entirely feasible will necessitate further study.

The differentiations given in the table are only comparative and show the instances in which higher concentrations and variable concentrations were necessary for the best differentiation. The observations emphasize the fact that it is not always with peptone that the best morphologic pictures are obtained. If the average differentiation is estimated from the higher differentiation values for the several peptones the value for peptone and proteose peptone is 2.54 and for tryptone 2.57. These values are practically equal, demonstrating that there is comparatively little difference in the value of these peptones. However, one factor is not considered, and that is pigment. The pigment of proteose peptone is often imparted to the growth, interfering with recognition of the inherent pigment of the organism. Sometimes the growth on proteose peptone is in excess of that desired, or the medium fails to liquefy properly. On the other hand, tryptone is a light-colored medium, which is of considerable value since it can easily be substituted for peptone. In fact, its clarity often makes it superior to peptone.

THE PHYSICAL CHEMICAL CHARACTERISTICS OF THE MEDIUM

The importance of physical chemical characteristics of the medium has been mentioned previously. These characteristics are surface tension, osmotic pressure and viscosity.

Surface tension is decreased on an increase in the concentration of peptones up to a certain point. It is possible that this property of peptones of decreasing surface tension is a reason for their serving so efficaciously in the nourishment of organisms. One needs only to recall the necessity of the reduction of surface tension either by the type of food one eats or by bile from the gallbladder in order to get proper digestion and assimilation of food in the duodenum. This reduction of surface tension, according to Gibbs' principle, would be most marked at the medium-organism interface, where the assimilation of nutriment takes place. This reduction would be interfered with by an excess of adsorbing interfaces of nonliving nature. Such adsorbing surfaces might be provided by carbonization in the autoclave. Naturally this feature would be variable and might influence not only the nutrient quality of the medium but also the availability of the nutriment.

Osmotic pressure is important not alone with reference to the medium but also with reference to the organisms. In plants this varies considerably. For example, it is much greater in desert plants.⁴ This is only natural, since the elevation of pressure as a result of a decrease in vapor pressure would decrease transpiration and prevent the plant

⁴ Fitting, Hans. *Ztschr. f. Bot.* 3:209, 1911. Livingston, B. E. *Plant World* 14:153, 1911.

from drying Green plants, however, are not identical with fungi, since in fungi there are neither arteries for the transport of nourishment nor cell spaces but merely a unity by individual cells Therefore, these individual cells are the factors in maintaining suitable osmotic pressure It has been observed that *Aspergillus niger* and *Penicillium* may develop an osmotic pressure as great as 157 atmospheres when grown in concentrated dextrose or saline solutions ⁵ Thus, several factors may play a part in the maintenance of sufficient osmotic pressure, with normal turgidity and function of the cell, the vapor pressure resulting from humidity and temperature, the movement of air and the relative osmotic pressure of the nutriment *Aspergillus niger* and *Penicillium* are comparatively more hardy than many of the pathogenic fungi and can meet the demanded variation probably more efficiently and without as much change as occurs in the latter organisms In addition, they do not show the variation in the morphology of the colony shown by many pathogenic fungi, which could well be influenced by the changes already mentioned

In order to test the effect of osmotic pressure on pathogenic fungi I planted organisms on W mediums containing the following concentrations of chemically pure sodium chloride 0.1, 0.5, 1 and 1.5 per cent ⁶ While the morphology was altered slightly in certain instances by increasing the osmotic pressure in this manner, the striking similarity of the colonies was not destroyed

Another factor not mentioned previously is viscosity In this work I have treated the physical chemical factors as though dealing with a liquid medium, when, in fact, I was employing a medium in which agar was used for solidification Because of the ready diffusibility of the liquid medium through the agar, this treatment was justifiable, since the units utilized by the organism were liquid and of the composition and ingredients, except for the agar, of the liquid medium Viscosity probably determines to some extent the availability of this liquid portion, since by an increase in viscosity there is an increase in the friction between the layers of fluids and less ease of their movements and diffusion This viscosity in mediums of higher concentrations apparently makes solidification by 1.5 per cent agar impossible My work on this subject has not shown sufficient results to be reported

With reference to surface tension, peptone mediums with dextrose have shown considerable variation ⁶ The most significant observation has been that the surface tension of peptone mediums containing 1 per

5 Atkins, W. R. G. Some Recent Researches in Plant Physiology, London, Whittaker & Co., 1916, p. 328

6 Williams, J. W. Physical Chemistry and the Growth of Certain Pathogenic Fungi, to be published

7-11 Footnotes deleted by author

cent dextrose is lower than that of mediums containing 4 per cent dextrose. My observations also indicate that when the ratio is maintained there is a significant correspondence of surface tension over a considerable range. The observations on surface tension also seem to check with the morphologic appearances. When the surface tension is lower, there is in the majority of instances a tendency to less aerial mycelium and less pleomorphism. Since W1 medium has a much lower surface tension than Sabouraud's proof medium one cannot ignore this variation. The advantage of greater concentration (possibly not beyond 8 per cent) of peptone when sugar is used may possibly be explained, at least in part, by this physical chemical characteristic. In most instances also an increase in sugar seems to increase both the surface tension and the pleomorphism. Of course, there is a coincident increase in the osmotic pressure, which I do not think has been completely ruled out. It is logical to assume that an increase in the surface tension would tend to push mycelium to greater lengths. With reference to subsurface mycelium, however, the explanation is not so tangible. As yet I do not think that I have a significant clue to its cause.

When the surface tension of Sabouraud's medium (S4) is lowered by means of sodium taurocholate,⁶ there is in many instances a tendency to frosting and development of coarse mycelium, similar to that on such mediums as W1, in which the ratio of peptone to dextrose is increased. These appearances seem better demonstrated with mediums with a surface tension of 52.5 dynes (28 C) or lower, since when one-half the concentration of W medium is used, with a resultant increase of surface tension of several points, the marked effects are not noted and the mycelium seems more aerial and less compact.⁶ Also, when the osmotic pressure of W medium is raised to 18.69 atmospheres (25 C) with sodium chloride,⁶ there is an increase in wetness and in some instances an increase in the area of frosting. At this osmotic pressure, however, no marked change was noted in the mycelium.

It will be necessary to use additional substances for lowering the surface tension and additional salts for increasing the osmotic pressure before any definite conclusions can be drawn with regard to the exact effects of surface tension and osmotic pressure. I am becoming increasingly aware of their importance in the morphology of the colonies of pathogenic fungi when peptones or amino-acids and dextrose are used. In bacteriology⁶ I think that they are equally important although there has been a tendency to forget them. A device for the measurement of surface tension, preferably an interfacial tensiometer, and a method for determining osmotic pressure, preferably by a study of the relative effect of the constituents of mediums and a substance of known molecu-

lar weight, such as sodium chloride, on cells,⁹ should be standard in every bacteriologic and mycologic research laboratory. In the latter test, if red blood cells are used one must realize that some constituents of the medium may have a hemolytic effect (but possibly due to surface tension) and that this effect may not be applicable to pathogenic fungi. Such an effect may be noted with certain salts, such as sodium taurocholate.¹²

COMMENT

In this paper I have attempted to emphasize the morphologic characteristics of certain pathogenic fungi. I think that this is justifiable, since there has been considerable recent emphasis on the microscopic characteristics of these organisms with reference to classification both from the point of view of methods of classification¹³ and from the point of view of practical identification by the laboratory worker.¹⁴ Another justification is the tardy appreciation of the importance of rough and smooth colonies of bacteria. Scientists seem to have been so enamored of the microscope and the microscopic picture that for many years they neglected what they could see with their eyes. I think that it is better to see first what one can with the naked eye and then, when completely satisfied with those observations, to resort to the microscope.

I have also emphasized the physical chemical properties of the mediums studied. I feel that this should be a function of every study of this nature. Not only this but also the fundamental chemical character of these organisms is important. The latter feature is being investigated by Dr. B. S. Gould, of my department, and will be reported later when a sufficient number of results are accumulated.

It is needless to say that variations of many of the colonies studied are very confusing. For example, *Trichophyton granulosum* grown on Sabouraud's proof medium showed a pleomorphic white growth. When transplanted to W1 medium the growth lost this pleomorphism, became radiate, with a covering like doeskin, and had a central area of dull raspberry. The question arises: Which is to be considered typical? It seems that the answer should be the growth on W1 medium. This stable morphologic picture for W1 medium does not always occur with

12 Williams, J. W. *Proc. Soc. Exper. Biol. & Med.* **27**: 913, 1930; **28**: 741, 1931.

13 Ota, M., and Langeron, M. *Ann. de parasitol.* **1**: 305, 1923. Vuillemin, P. *Compt. rend. Acad. d. sc.* **180**: 102, 1925. Guiart, J., and Grigorakis, L. *Lyon med.* **141**: 369, 1928. Grigorakis, L. *Ann. de dermat. et syph.* **10**: 18, 1929. Emmons, C. W. *Dermatophytes: Natural Grouping Based on the Form of the Spores and Accessory Organs*, *Arch. Dermat. & Syph.* **30**: 337 (Sept.) 1934.

14 Shaw, F. W. *J. Lab. & Clin. Med.* **20**: 113, 1934.

the first transplant. It appears that the morphologically variable organisms must reach their stride for the particular medium, and if stability is to be reached the medium must be one of stabilizing character on which the organism shows no variation or easily recognizable morphologic variations. Thus, the character of an organism may vacillate from transplant to transplant from one easily recognizable type of colony to another.

I have had the opinion that a medium of a ratio of constituents fairly near that of the skin might be desirable, and in W medium the tendency is in that direction. It is probable that horn, skin or hair might be better, but technical difficulties are encountered. I am having digests made of hair, and I am growing organisms on horn, hoof and skin in an effort to assess their merit.

Some of the pathogenic fungi have been looked on by many workers with too much awe. For example, speaking from experience with W1 medium, it seems that p_H has been overemphasized. Apparently a considerable variation of osmotic pressure is allowable, and certainly plenty of concentration of the medium is permissible as long as the same ratio is maintained.

Amino-acids as substitutes for peptone may be pure, but they are expensive and at present are limited largely to research work. There is some indication that ratio and surface tension may act the same, at least in some amino-acids, as they do in peptone. Apparently some organisms do not relish certain amino-acids, at least, their application to the cultivation of organisms is not as wide as that of peptones. This limits their use, except when time and expense are minor items. Therefore, why not adapt peptones, if this is possible, for practical every-day use and reserve consideration of the amino-acids for special occasions? This also applies to synthetic mediums in which amino-acids are not ingredients.

SUMMARY

The variation of the morphology of the colony with a change of the ratio of dextrose to peptone, proteose peptone or tryptone with reference to physical chemical characteristics has been discussed.

The advantages of mediums of a ratio different from that of Sabouraud's proof medium were cited. A medium of 4 per cent peptone, 1 per cent dextrose and 1.5 per cent agar, with a p_H which may vary from 5.2 to 8, is considered of great value.

Methods of estimating the differentiation of colonies were suggested. Morphologic stabilizing effects of mediums were discussed.

An attempt was made to divide the organisms according to the morphology and the production of pigment.

A correlation of surface tension, osmotic pressure and morphology of the colony was drawn. The possibility of variation of the morphology on variation of the asparagine-dextrose ratio was advanced as a result of preliminary work. Here, too, a variation of the surface tension similar to that seen when the peptone-dextrose ratio is changed was noted.

The importance of a standard device for estimating surface tension and a standard method for measuring osmotic pressure in every research, bacteriologic and mycologic laboratory was emphasized.

References were given which will serve as a key to the literature.

HISTOPATHOGENESIS OF PSORIASIS AND ITS ABERRANT LESIONS

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Psoriasis has been accepted as a clinical and histologic entity. The identity of the condition has been conceded. Yet in carefully investigated cases of psoriasis the involvement has eventuated in other conditions, mycosis fungoides, for instance. At times it is difficult, even impossible, to differentiate clinically between psoriasis and certain other scaling dermatoses, such as eczema, the prefungoid stage of mycosis fungoides, syphilis, lupus erythematosus, generalized superficial epitheliomatosis cutis, lichen planus, pyoderma and other conditions. Not infrequently it is equally difficult or impossible to make an unequivocal diagnosis in the laboratory. In many cases of typical psoriasis there are individual lesions that alone do not suggest psoriasis. The object of this investigation is a clinical and microscopic study of borderline cases of psoriasis, atypical psoriatic lesions, eruptions in patients with typical psoriasis and uncommon and rare examples of the disease in an attempt to confirm or refute the identity of the disease and to broaden or narrow the conception of it as a clinical and histologic entity.

The history of the study of the pathology of the cutaneous organ is of great interest and has a direct bearing on the subject matter of this paper, therefore, we shall attempt to sum up briefly the essential facts available.

The Greek physicians of the Attic period brought forth the hypothesis that the fluids of the body were responsible for all dermatoses. This influence limited dermatologic knowledge until leprosy was definitely found to be controlled only by isolation. Opinions change slowly, and it was only with the help of an epidemic of syphilis which swept from country to country that an outside causative factor was considered for the dermatoses. In the early part of 1700 physicians

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Read before the Section on Dermatology and Syphilology at the Joint Session of the American Medical Association and the Canadian Medical Association, Atlantic City, N. J., June 12, 1935.

began in a crude way to formulate classifications and recognize many of the dermatoses as they are known today

It remained for Willan¹ (1798) to classify the dermatoses seriously. He did this purely from a morphologic standpoint, placing in a few main groups multiple entities with polyvalent etiology. The classification was suitable for that period but was gradually outmoded owing to constantly increasing knowledge. Entity after entity was removed, leaving an almost unrecognizable skeleton.

Von Hebra² was responsible for two great advances in dermatology. First, he was instrumental in causing the skin to be considered as an organ of the body capable of having its own functions and diseases, and, second, he was credited, in conjunction with Rokitansky,³ with having fathered cutaneous pathology. They were followed by Virchow⁴. Unna⁵ to whom is due so much credit in the advancement and dissemination of histopathologic knowledge, published his detailed work in 1894. Munro⁶ (1893-1898) added to the histopathology of psoriasis by describing the Munro-Sabouraud micro-abscesses and explaining their formation. Haslund⁷ (1912) reviewed the literature and described 9 cases of psoriasis in detail. He gave the views of various contemporary workers whose opinions concerning the histopathogenesis of the psoriatic lesion were at great variance. Civatte⁸ (1924) gave an excellent differ-

1 Willan, R. *On Cutaneous Diseases*, Philadelphia, Kimber & Conrad, 1809, *Die Hautkrankheiten und ihre Behandlung systematisch beschrieben*. Aus dem Englischen übersetzt, und mit einigen Anmerkungen und einem Anhang begleitet von Friedrich Gotthelf Friese, Breslau, J. F. Korn, 1799-1806, *Delineations of Cutaneous Diseases*, edited by Thomas Bateman, London, Longman, Hurst, Rees & Company, 1817.

2 von Hebra, H. *Morbid Changes of the Skin and of Its Appendices with Their Relations to Diseases of the General Organism*, translated from the German by M. Hirschfeld and A. Feinberg, St. Petersburg, Ettinger, 1885.

3 Rokitansky, C. *Handbook of General Pathological Anatomy*, Vienna, Braumüller & Seidel, 1842-1846.

4 Virchow, R. L. K. *Cellular Pathology as Based upon Physiological and Pathological Histology*, translated from the second edition by Frank Chance, New York, R. M. DeWitt, 1860.

5 Unna, P. G. *The Histopathology of the Diseases of the Skin*, translated from the German by Norman Walker with the author's assistance, New York, Macmillan & Co., 1896.

6 Munro, W. J. *Note sur l'histo-pathologie du psoriasis*, *Ann de dermat et syph* 9: 961, 1898.

7 Haslund, P. *Die Histologie und Pathogenese der Psoriasis*, *Arch f Dermat u Syph* 114: 427 and 745, 1912.

8 Civatte, A. *Psoriasis and Seborrhoic Eczema*. *Pathology, Anatomy and Diagnostic Histology of the Dermatoses*, *Proc Roy Soc Med (Sect Dermat)* 18: 1, 1924.

entiation of psoriasis and seborrheic eczema from a histologic point of view Barber⁹ (1930) did much to clear up the status of the pustular lesions in psoriasis

The era of dermatologic influence is widening Allergy, physiology, chemistry, histopathology and endocrinology are essential in the evaluation of the dermatoses and their causation

In this work we studied the histopathologic changes in an attempt to determine the histopathogenesis of psoriasis and its related conditions, well realizing that few cutaneous lesions present typically pathognomonic diagnostic criteria, but if reports of other authors are to be relied on psoriasis is one condition which does have a fairly characteristic picture Therefore, we have taken typical psoriatic lesions on the one hand and aberrant lesions of patients with psoriasis on the other in an attempt to establish

- 1 A basic histopathologic formula for typical psoriasis
- 2 The relationship of the aberrant lesions to the typical formula
- 3 The frequency of aberrant lesions
- 4 The status of psoriasis among the inflammatory dermatoses

In order to make a diagnosis of psoriasis, one should follow a routine system of examination beginning with the scalp, mucous membranes, elbows, knees, genitals, extremities and trunk The following features should be evaluated in making the diagnosis

- 1 *Tache de bougie* (white silvery powder)
- 2 *Rosni sanglante* of Auspitz (bleeding points)
- 3 Sites of predilection
- 4 Symmetry
- 5 Lesions on the extensor or flexor surfaces
- 6 Type of scaling
- 7 Amount of infiltration
- 8 Duration and history of previous attacks
- 9 Familial history of psoriasis

The basis of a study of aberrant lesions would of necessity rest on a similar study of typical lesions which preferably should be from the same patients but would be of equal value if from patients with no atypical lesions Therefore, we have studied 150 cases of psoriasis histologically In 50 of these cases histologic sections were taken from undeniably typical psoriatic lesions and from typical psoriatic sites Each

⁹ Barber, H W Acrodermatitis Continua Vel Perstans (Dermatitis Repens) and Psoriasis Pustulosa Brit J Dermat 42:500 (Nov) 1930, Pustular Psoriasis of Extremities Proc Roy Soc Med (Sect Dermat) 26:329 (Feb) 1933

case was passed on by three qualified dermatologists before a specimen was taken for section. With these sections forming a basic structure or formula, we were able to compare the aberrant lesions of 100 patients with those of patients with typical lesions and from these draw our conclusions.

In the basic histopathologic formula for typical psoriasis we have found the following essential points in the relative rate of occurrence. Charts were kept to note every change from normal, and therefore each item will be referred to on a percentage basis. Beginning at the outermost layer we found that the silvery laminated scales were composed for the most part of hyperkeratosis and, to a much less degree, of parakeratosis, which tended to be patchy and alternated with the granular layer. We found a dry, irregular, moderately thickened epidermis. The epidermis is referred to as dry, although the intercellular lymph spaces of the rete Malpighii were widened and moderate exocytosis and exoserosis were constantly in progress. The prickle cells appeared pale and sometimes swollen, often the degeneration progressed until the nuclei became flattened or crescentic and migrated to the edge of the cell, constituting hydropic degeneration. These cells were shed as the underlying epidermal cells proliferated. The complete absence of keratohyalin, with the formation of an imperfectly keratinized granular layer, was not a conspicuous feature. The parakeratosis alternated with the granular layer in 44 per cent of the cases and was sparse, that is, in small areas, in 30 per cent. The so-called Munro-Sabouraud abscesses, which are composed of broken-down cellular elements, were present in 36 per cent of the cases studied. A loose interpretation was placed on these abscesses, including grouped cellular detritus in the lamellae of the horny layer as well as similar collections lying between the outer corneous layer and the upper layer of prickle cells, in 24 per cent of the cases these were just below the horny layer and in 12 per cent, in the horny layer. We found the granular layer well developed in 24 per cent of the cases, intermittent in 44 per cent and absent in 12 per cent. Spongiosis was absent in all sections, but in 2 sections small vesicles were found. The basal layer was present and disorganized over a few papillary bodies in 56 per cent.

The rete pegs were irregularly acanthotic and elongated and tended to be polymorphic, some thin, some thick and others fused, and in 16 per cent of the sections the papillae appeared to be particularly tortuous. We believe that this observation was a feature of acanthosis and not the result of an oblique cut of the section, as some of the sections with tortuous papillae were cut on many different angles, yet the same picture was obtained.

The papillary bodies presented moderate edema in 52 per cent of the sections and marked edema in 24 per cent. These bodies tended to be irregular in size and club-shaped. There was moderately severe dilatation of the vessels of the papillary bodies, with sparse round cell infiltration.

The upper layer of the cutis was involved in the edematous process in 100 per cent of the sections, the involvement extending down to the middle layer of the cutis. Interstitial edema predominated over parenchymatous edema. The collagen bundles were swollen in a majority of the sections and dissociated in a few. The lymph spaces tended to show moderate dilatation in 32 per cent of the sections and marked dilatation in 52 per cent, the vessels being dilated accordingly. The walls of the vessels were normal in 90 per cent of the sections. The infiltration of the upper layer of the cutis was focal in 92 per cent and diffuse in 28 per cent.

The adnexa was unaffected. The fat was normal in 98 per cent of the sections, fatty infiltration being present in 2 per cent.

RELATIONSHIP OF THE ABERRANT LESIONS TO THE TYPICAL FORMULA

Psoriasis is a well defined dermatosis, but in about 1 of 6 cases there are eruptions less monomorphic in clinical type and distribution which confuse the picture. They frequently occupy the sites which psoriatic lesions tend to avoid. The elementary lesions are either of brighter or of duller erythematous tone. The lesions may be exudative or dry, smooth with no scaling or covered with fine micaceous scales or heavy coarse crusts, impregnated with oily substance or devoid of the oily factor but all with the erythemosquamous element. Some lesions clinically resemble psoriasis closely, others little or not at all. We observed lesions ranging in appearance from that of eczema madidans to the fine white scaling of pityriasis alba. It is self-evident that there must be some relation between the various types of aberrant lesions and the typical lesions of psoriasis which each patient presented.

1 *Lesions of an Eczematous Type*—These lesions were present in a group of 26 cases, or one-fourth the number studied. We placed in this group the cases in which indefinite lesions were present for which no other diagnosis could be entertained. The lesions were of the dry and weeping, erythematous, infectious, crusted and scaling types, none of which, if taken alone, would have been diagnosed psoriasis. We found that in this group the lesions definitely had a different histologic picture in many respects. The epidermis was moist in 32 per cent of the lesions in these cases against 2 per cent of the cases of psoriasis. The thickness of the suprapapillary layer tended to be normal. Para-

keratosis was patchy or sparse. The granular layer was better developed (40 per cent). Acanthosis was somewhat more general. Spongiosis was noted in 28 per cent of the sections against none in those of psoriasis. Vesicles were found in 24 per cent of the sections. The papillary bodies and the subcutis showed less edema, and the vessels did not show the marked dilatation so generally found in the formula for psoriasis. The difference lay mainly in the epidermis.

2 *Lesions Resembling Seborrhea*—These were noted in 16 cases. The lesions were taken for the most part from the axillae, chest and scalp and presented yellowish, greasy, branny scales on an erythematous, maculopapular base.



Fig 1—Photomicrograph of an aberrant lesion of typical psoriasis showing superficial dermatitis with no epidermal changes (simple dermatitis)

The question always arises when one discusses psoriasis and seborrhea as to whether the conditions are distinct clinical entities which closely simulate each other, coexisting in the same soil with some lesions clinically indistinguishable, whether one is the stepping-stone or precursor of the other or whether they are phases of the same disease, one being in an intermediate stage at the time of clinical observation. The same may be said concerning all other types of aberrant lesions.

We found that the lesions which closely resembled seborrhea had a pathologic picture that fits in midway between the formula for typical psoriasis and the picture in our 26 cases of the eczematous type. The main characteristics were spongiosis with the formation of vesicles in 20 per cent of the sections, the striking similarity in amount and type of parakeratosis and, in general, the lessened edema of the upper portion of the cutis and the papillary bodies. The change appears to be more

confined to the epiderm than that seen in psoriasis. The grouped sub-corneal collection of cellular elements was present in 20 per cent of the sections.

3 *Lesions Resembling Circumscribed Neurodermatitis (Lichen Chronicus Simplex)*—Ten cases were studied. The clinical picture in this group was that of an erythematous, infiltrated, thickened, lichenified, slightly scaly patch, often with smaller corymbiform lesions about the edge of the main plaque. This type of lesion was common over the sacrum just above the intergluteal fold.

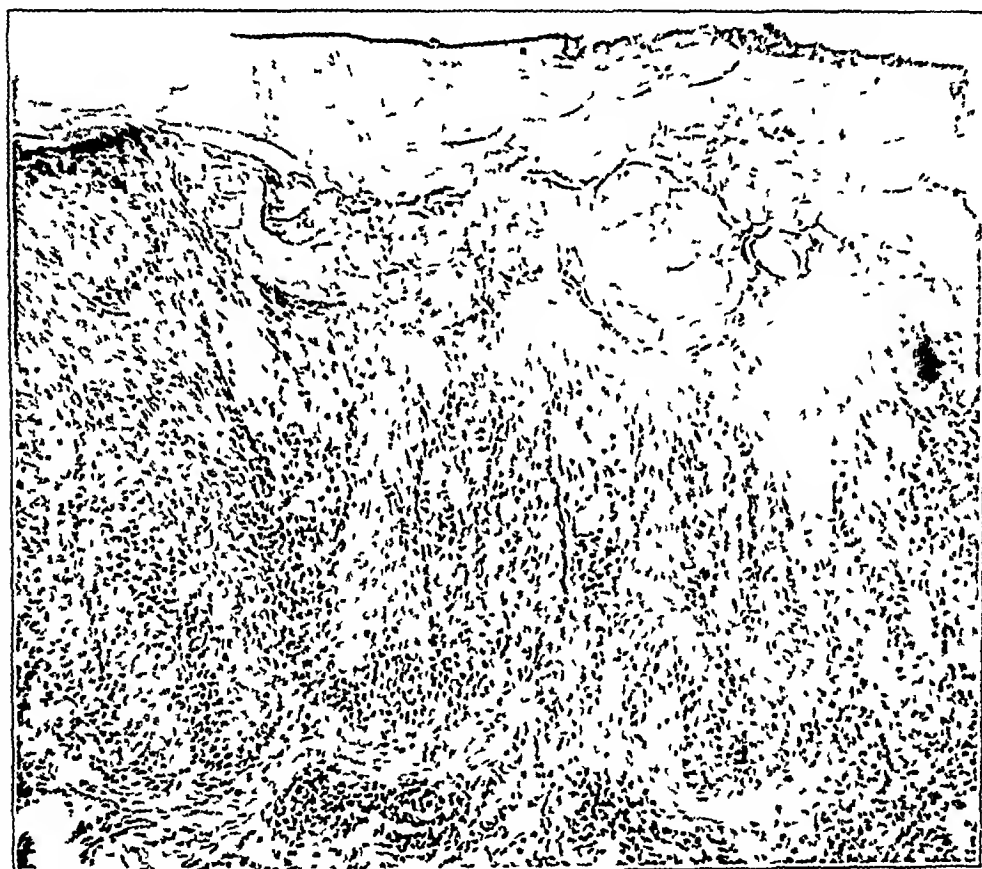


Fig. 2—Photomicrograph of an aberrant lesion of typical psoriasis showing superficial dermatitis with eczema-like changes in the epidermis.

Histologically the lesions were predominantly dry with an increased granular layer. Acanthosis was more general than in the cases of psoriasis, and the edema of the papillary and subpapillary area was less. One section showed slight spongiosis and formation of vesicles, which was a long-standing chronic process. Numerous Mouton abscesses were noted in 2 of our 10 cases. The lesions differed from those of psoriasis mainly by the thick granular layer.

4 *Pustular Psoriasis*—Nine cases were studied. Before the discussion of the changes noted in the sections, brief mention will be made of the history of the condition as an entity.

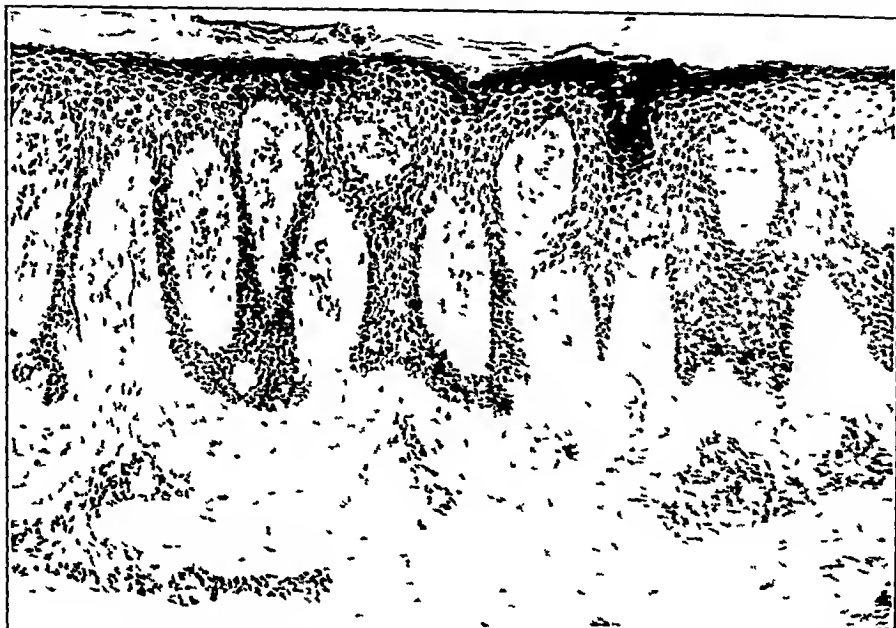


Fig 3—Photomicrograph of an aberrant lesion of typical psoriasis showing superficial dermatitis plus epidermal changes of the dry type simulating neurodermatitis



Fig 4—Photomicrograph of an aberrant lesion of typical psoriasis showing superficial dermatitis plus epidermal changes of the dry type plus occasional vesicles simulating seborrheic dermatitis

Strandberg¹⁰ was the first to suggest that pustular lesions might be a feature of psoriasis. Baiber⁹ in 1930 gave an excellent discussion of this subject, reporting 4 cases, 2 of which were classed as instances of acrodermatitis perstans and 2 as cases of pustular psoriasis. Regarding the former, he favored using the terminology of Dore,¹¹ "acrodermatitis perstans," rather than "acrodermatitis suppurativa continua" of Hallopeau¹² or "dermatitis repens" of Crocker.¹³ He made an absolute distinction between pustular psoriasis and acrodermatitis perstans of Dore. There has been considerable recent literature on the subject, which need not be reviewed here.

The clinical picture of pustular psoriasis is usually consistent. There is a vesiculopustular squamous eruption, primarily affecting the thenar area of the palms and central inner portion of the soles and from these original sites spreading to adjacent areas. The pustules dry up, some form brownish translucent dots the size of a pinhead, and others form crusts or scabs and are desquamated, leaving a reddened, angry, denuded epidermis. There are exacerbations and remissions. During an exacerbation there may be sensations of pruritus, heat and even dull "drawing" pain. Mycologic and bacteriologic examinations always give negative results. The condition may be accompanied by interdigital dermatophytosis which obscures the clinical picture.

In all but 3 of our cases there was concomitant psoriasis or a past history of psoriasis.

The histologic picture in these cases varies somewhat according to the condition of the horny layer and the age or stage of the condition. There was evidence of chronic eczema in 4 of the cases.

The vesiculopustules in the upper layer of the epiderm were filled with coagulated serum and some leukocytes. The rete pegs were irregularly acanthotic, and the acanthosis tended to include the suprapapillary plates. However, in all 9 cases there was an intense leukocytic infiltration of the upper portion of the cutis and also of the epiderm. This intense leukocytic infiltration appeared to be attracted to the surface of the epidermis, where small and large collections of leukocytes occurred, forming abscesses which are best known as Monro-Sabouraud abscesses and may become large enough to be seen by the naked eye. These collections of leukocytes and degenerated epithelial cells occur

10 Strandberg, J. Acrodermatitis continua (Hallopeau). *Acta dermat.-venereol.* 6:314 (Oct.) 1925.

11 Dore, S. E. Notes on Cases of Chronic Mild Localized Type of Acrodermatitis Perstans. *Brit. J. Dermat.* 40:12 (Jan.) 1928.

12 Hallopeau, H. Sur la production consecutivement a des plaques psoriasiques d'achromies persistantes. *Bull. Soc. franç. de dermat. et syph.* 3:11, 1892.

13 Crocker, H. R. *Diseases of the Skin*, ed. 3. Philadelphia: P. Blakiston's Son & Company, 1903.

however, in other conditions than psoriasis and should not be taken as a pathognomonic criterion. They are frequently found in lesions of eczema, and recently Sulzberger¹⁴ found that the application of extract of poison ivy to sensitized guinea-pigs will produce typical Monro-Sabouraud abscesses. This observation at least proves that this particular phase of the psoriatic picture can be of exogenous etiology. The explanation for this phenomenon was best described by Civatte.⁸ A group of migratory cells emerge from a vessel at the summit of a papilla and open a passage through the rete mucosum which is disintegrated by their transit. At the point where this is about to occur, the malpighian cells become swollen and mass together. Their borders become less distinct, and there is considerable intercellular edema. It follows, then, that the dictum of Sabouraud—that the exocytosis of psoriasis is dry and without exoserosis—cannot be fully accepted. In this swollen and softened mass emigrated cells dig a sort of tunnel toward the surface, by which they ascend toward the upper layers of the rete. This tunneling is not the only way exocytosis takes place. Throughout the area polymorphonuclear leukocytes are seen between the swollen epithelial cells which form the walls of the tunnel, ascending the softened rete layer without tearing it. Having reached the upper malpighian layer the migratory cells encounter a barrier formed by the more or less keratinized layers, and the cells spread out like a column of smoke held down by an obstacle.

In our other 6 cases, constituting 66 per cent of the group, there were positive signs of psoriasis. Dr David L. Satenstein, to whom we are indebted for help in the examination and interpretation of the histologic sections used in this work, holds that pustular psoriasis is a misnomer and that the picture is that of chronic eczema and not one of psoriasis. Many others also hold this view. Andrews and his associates¹⁵ expressed the opinion that the histologic picture is not distinct enough for one to make a diagnosis without other signs of psoriasis being present. On the other hand, Dr Alexander Fraser, who also gave his interpretation of the histologic sections in this work, believes definitely that these cases of pustular psoriasis can be diagnosed histologically. It should be noted that he has been able to demonstrate this many times.

The high papillae and very thin suprapapillary plates coupled with the extreme dilatation of the vessels, the parakeratosis, which is patchy and intermittent, and, finally, the collections of pus lead us to believe that pustular psoriasis is a definite type and belongs with the syndrome

14 Sulzberger, M. Personal communication to the authors.

15 Andrews, G. C., Birkman, F. W., and Kelly, R. J. Recalcitrant Pustular Eruptions of Palms and Soles, *Arch. Dermat. & Syph.* 29: 548 (April) 1934.

of psoriasis as one of its many manifestations. Its name is not material, any name linking it to psoriasis is sufficient.

5 *Lesions of Intertriginous Nature*—Nine cases were studied. The lesions may be described for the most part as being erythematous, eczematoid, macerated and often fissured, occurring in the usual intertriginous areas, notably beneath the breasts, in the cural region and in the intergluteal fold. In our experience such intertriginous lesions occur much more frequently in cases of psoriasis than in cases of other cutaneous disorders.

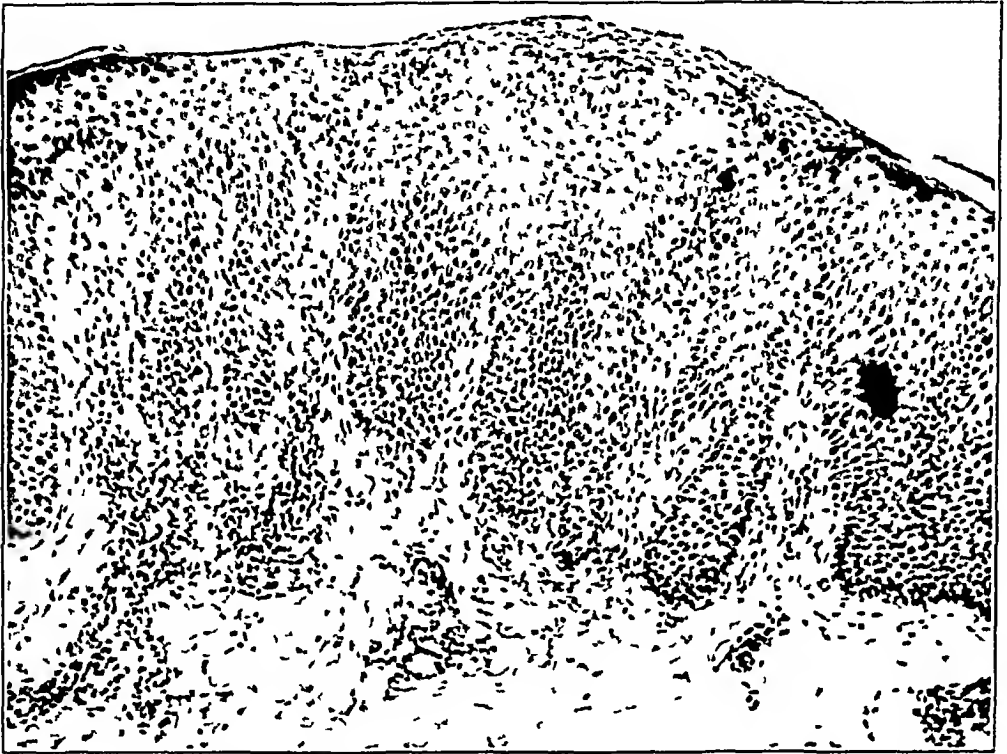


Fig 5—Photomicrograph of an aberrant lesion of typical psoriasis showing superficial dermatitis plus epidermal changes of the dry type plus parakeratosis simulating chronic eczema.

The sections observed, although the condition in practically all the cases was diagnosed as chronic eczema, did have many features of psoriasis. However, the pathologic picture had been altered, so that in 30 per cent of the sections spongiosis and vesiculation were noted even though the granular layer was intact throughout other portions of the slide. Therefore, the condition in this group at least will have to be classed histologically with the eczemas primarily. It is interesting to note that in some of the cases, in which a typical psoriatic patch extended into the intergluteal fold a section taken from the macerated area showed a histopathologic picture corresponding to the picture of eczema seen in other sections.

6 *Lesions of a Papulo-Erythemasquamous Nature*—A study was made of 9 cases. The lesions included ill defined erythematous, dry, scaly lesions of polymorphic clinical character which loosely resembled those of parapsoriasis.

These lesions, although clinically resembling each other, had extremes in pathologic pictures, ranging from practically no histologic changes through eczema into the dry type of lesion found in neurodermatitis. Therefore, this group will be discussed more in detail with the summation of observations on the aberrant lesions.

7 *Lesions of Lichenoid Character*—Eight cases were studied. This group included cases of lesions simulating lichen planus and the other

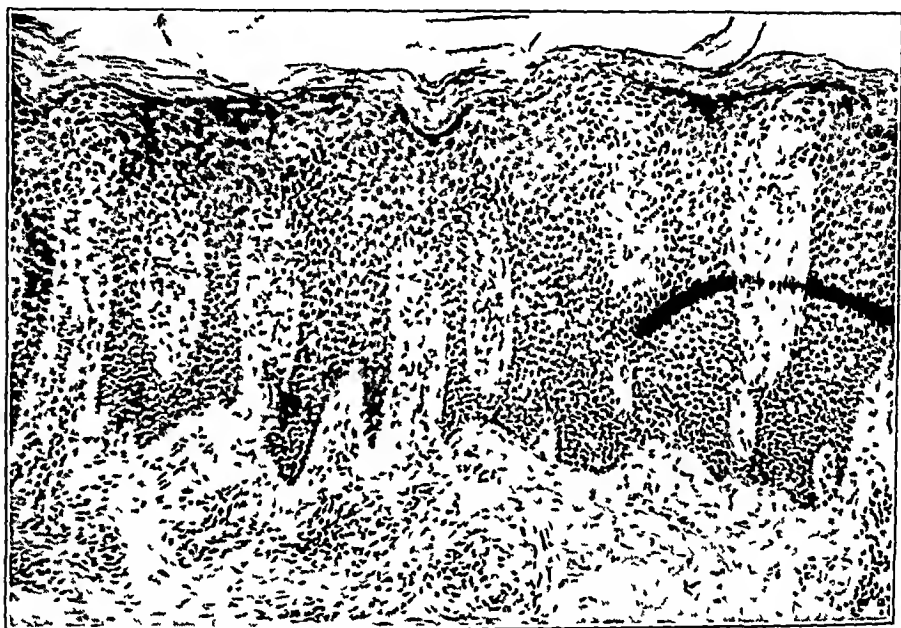


Fig 6—Photomicrograph of an aberrant lesion of typical psoriasis showing superficial dermatitis plus epidermal changes of the dry type plus parakeratosis plus characteristic dilated vessels and papillary bodies simulating psoriasis.

lichen, including pityriasis rubra pilaris. There were 3 cases of concomitant lichen planus with long-standing psoriasis. In 1 case there was a history of lichen planus-like papules occurring each spring over a period of several years, many cases of this type have been reported. The pathologic picture of the lesions of lichen planus was that of typical lichen planus. However, the sections of lesions on the elbow in 2 cases showed the histologic architecture of chronic eczema, although the clinical picture was that of typical psoriasis. In the third case the specimen studied showed the structure of lichen planus. This phenomenon will be discussed later, under altered cutaneous resistance.

Pityriasis rubra pilaris has many features in common with psoriasis, with which it coexists or alternates often at its inception. We found coexisting pityriasis rubra pilaris in 1 case, with typical psoriasis elsewhere. Other cases have been reported by Wigley, Little,¹⁶ Davis, Drosty and Prieto¹⁷

The lesions in this group presented a variety of histologic pictures, however, they were all dry, a well developed granular layer predominated and in some sections parakeratosis was present but sparse. The papillary and subpapillary zones showed moderate lymphocytic infiltra-

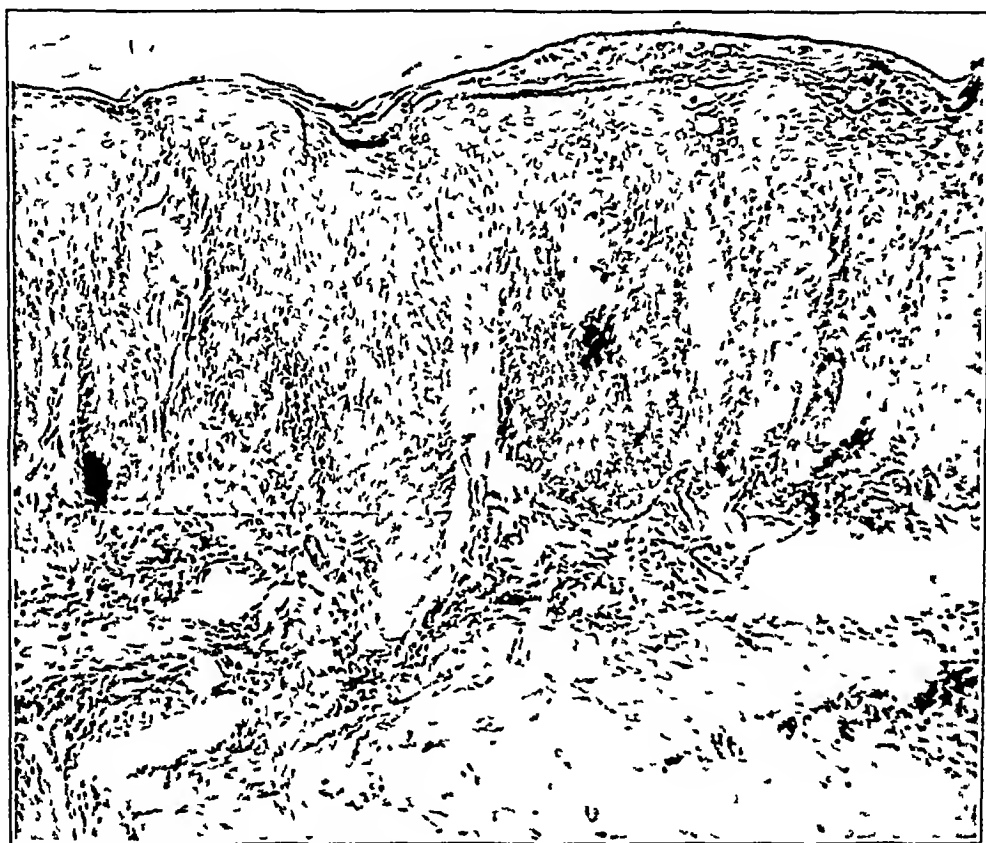


Fig 7—Photomicrograph of an aberrant lesion of typical psoriasis showing superficial dermatitis plus epidermal changes of the dry type plus parakeratosis plus characteristic dilated vessels and papillary bodies plus exfoliation of the epidermis (exfoliative dermatitis)

tion except in the 3 cases of typical lichen planus, which were excluded from this summation. The cause for the variation in histologic structure in similar clinical lesions will be discussed later.

16 Little G. Psoriasis Simulating Lupus Erythematosus, Tr. M. Soc. London 30:384, 1906-1907.

17 Prieto J. G. Relation of Psoriasis to Pityriasis Rubra Pilaris. Case. Actas dermo-sif 26:345 (Feb.) 1934.

8 *Lesions of a Nodular Character*—The nodular lesions were studied in 5 cases which comprise the group in which the lesions were distinctly infiltrated, nodular and even fungoid. One of these cases was that of a private patient of Dr Frank Fraser and Dr Alexander Fraser, who was presented before the New York Dermatological Society and who had typical mycosis fungoides on what appeared to be psoriasis of many years' duration. (This case will be reported in detail by them later.) However, we can say that several specimens had been taken from this patient in the past, and all had shown only psoriasis, with no evidence of mycosis fungoides. Nodular lesions have a predilection

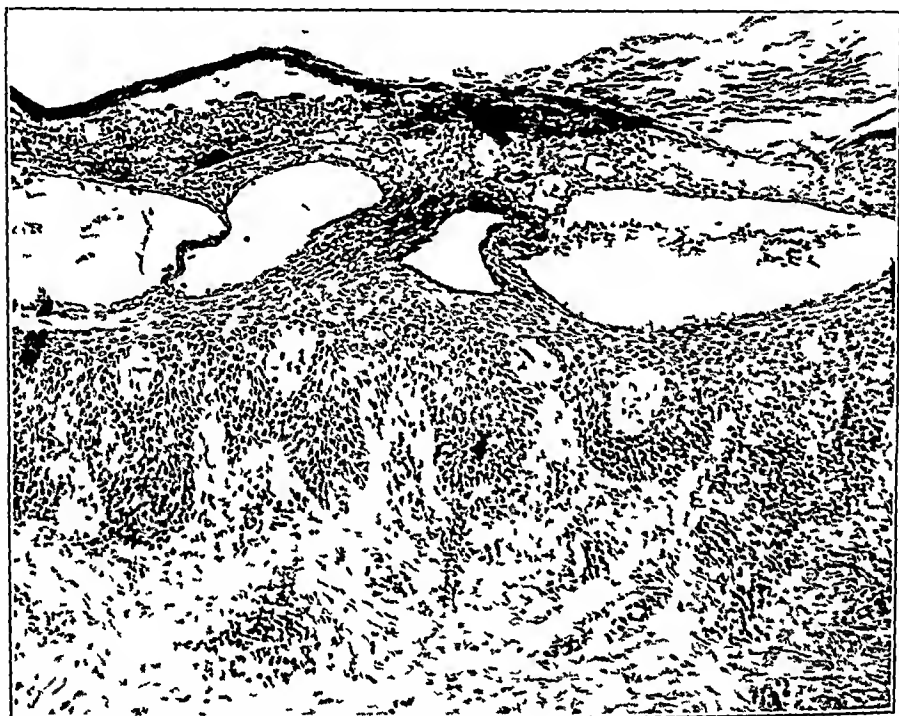


Fig 8—Photomicrograph of pustular psoriasis of the palms associated with typical psoriasis elsewhere

for the extremities, although occasionally one may be found on the trunk. The histopathologic change is not sufficiently distinctive to place the cases in a separate group entity. The lesions in our cases had features of eczema, 50 per cent showing spongiosis and formation of vesicles. A characteristic feature of psoriasis is severe edema of the papillary bodies and upper and middle portions of the cutis, with a tendency to regular acanthosis of the rete pegs. Therefore, again we had a group of cases in which the condition did not resemble psoriasis completely yet retained some of its main features.

9 *Lesions of Palms and Soles Suggesting Keratoderma*—In 4 cases of 100 there was a characteristic thickened, rough, somewhat verrucous appearance of the palms and soles. Clinically the condition resembled true keratoderma palmare et plantare. There was typical psoriasis elsewhere in all cases.

The characteristic feature of the sections was a greatly thickened hyperkeratotic layer with a well developed granular layer. In 1 section small vesicles without spongiosis were noted at the summit of the rete peg. The rete pegs were regularly acanthotic in 75 per cent of the sections, with the papillary bodies remaining comparatively normal, giving the appearance of elongated papillae. There were features of psoriasis and also features which suggested keratoderma palmare et plantare. In 1 case vesicles were present without spongiosis.

10 *Lesions Resembling Lupus Erythematosus*—Two cases were studied histologically. The lesions simulated the clinical characteristics of lupus erythematosus. They were sharply defined, oval or circinate, erythematous, slightly scaly patches of various sizes. Frequently, owing to an element of seborrhea, the clinical diagnosis became difficult. In 1 case the section showed typical lupus erythematosus, with thinned epithelium, basophilic degeneration, loss of elastic tissue and edema of the cutis. In the other the lesions were those of the dry type of chronic eczema.

11 *Exfoliative Dermatitis Following Psoriasis*—Two cases were studied. There was marked resemblance to the picture of psoriasis with an increase in mitotic figures in the epidermis and an increased infiltration of lymphocytic cells and connective tissue cells in the papillary and subpapillary zone. The picture was not distinctive and could not be differentiated from that of exfoliative dermatitis resulting from eczema, pityriasis rubra pilaris or any of the other conditions eventuating in exfoliation.

COMMENT

Over 600 patients were thoroughly examined for aberrant lesions, and among this number 100 were found with lesions abnormal enough to be placed in one of the groups described. Therefore we found on the average 1 patient of 6 presenting aberrant lesions of psoriasis with typical lesions elsewhere.

To summarize briefly the total observations on the aberrant lesions, we found that there were several clinical groups in which a somewhat uniform histologic picture was present subject to slight variations. The group with eczematous characteristics presented superficial dermatitis with eczematoid changes. The lesions presented by the group with seborrhea were drier than those of the group with eczema but still showed signs of eczema. In 24 per cent of the cases vesiculation was

present and in 15 per cent, spongiosis. The granular layer was prominent in most sections. The lesions of the group with circumscribed neurodermatitis were uniform, with an increased granular layer, but the histologic picture of the papillary bodies and subpapillary layer varied greatly, ranging from no change to greatly dilated vessels and interstitial edema. In 4 of the cases of pustular psoriasis there was a picture of acute eczema with intense exudation, and in the remaining 5, an almost classic picture of psoriasis. The lichenoid, papulo-erythemasquamous, keratoderma, lupus erythematosus, nodular and exfoliative types were greatly in the minority in frequency of occurrence, and the histologic pictures were polymorphic.

In 1 case the nodular lesions deserve special mention. The patient for many years had had what had been diagnosed by many competent dermatologists as psoriasis. The lesions were not pruritic but became so following roentgen therapy. A specimen was taken for section in February 1935, and the slide showed psoriasis. Two weeks later, fungoid lesions appeared in several areas, and sections from these areas gave a picture of mycosis fungoides characterized by mitotic figures and irregularity of size, shape and staining qualities of the nuclei and protoplasm of the newly formed reticular cells. There was a definite reticulum about each of the cells. We call attention to this phenomenon of mycosis fungoides occurring in patients with clinical psoriasis because since the study was begun, many dermatologists have commented on this singular occurrence in their own experience. A considerable number of cases of this type have been reported. Therefore, it must occur more frequently than is generally supposed.

Keeping in mind local and external modifying influences on the disease in the same patient, it seems impossible that most of the atypical lesions were not related in some way to the typical psoriasis which each patient had. Therefore, it would seem logical that the aberrant lesions offer a connecting link between psoriasis and the other superficial inflammatory dermatoses. Surely the soil and etiology in many instances were the same for the aberrant as for the typical lesions. Many of the aberrant lesions had the typical distribution of psoriasis, and their evolution presented the same physiologic problems.

We are forced to assume that the difference in the clinical and in the histopathologic picture lies in one or more of the following causes:

- 1 The pressure resistance of the various anatomic segments of the skin had become altered, changing the clinical and the histologic picture.

- 2 We were dealing with a transient stage of psoriasis.

- 3 There was an unusual or altered concentration and distribution of the toxic principle.

4 There were variations in local resistance, due to the site of the lesions or to exogenous causes, such as friction, moisture, heat and treatment.

If it is possible to have one or more aberrant lesions caused by any one of the aforementioned causes, is it not possible to have the same factor act generally and change the entire clinical picture but still have the same fundamental etiologic factor?

Heimann¹⁸ stated that eczema does not differ from the other fibrous lymphocytic inflammations except in the histologic peculiarities occasioned by its site

Psoriasis, by reason of its fixed clinical and histopathologic picture, is the normal reaction to an abnormal stimulus, and by the same reasoning we can say that eczema, because of its polymorphic character, is a variation from the normal reaction. Therefore, psoriasis is not a disease but a cutaneous reaction governed by the factors previously mentioned. This applies equally to the other superficial dermatoses. Psoriasis, although not a disease, is an entity because of its fixed type of cutaneous reaction, giving in the majority of cases a typical clinical and histologic picture.

A classification according to the following outline is consistent with the actual histopathologic findings of the aberrant lesions

- 1 Superficial dermatitis with no epidermal changes (simple dermatitis)
- 2 Superficial dermatitis plus eczema
- 3 Superficial dermatitis plus epidermal changes of the dry type simulating neurodermatitis
- 4 Superficial dermatitis plus epidermal changes of the dry type plus an occasional vesicle (seborrheic dermatitis)
- 5 Superficial dermatitis plus epidermal changes of the dry type plus parakeratosis (chronic eczema)
- 6 Superficial dermatitis plus epidermic changes of the dry type plus parakeratosis plus characteristic dilated vessels and papillary bodies (psoriasis)
- 7 Superficial dermatitis plus epidermal changes of the dry type plus parakeratosis plus characteristic dilated vessels and papillary bodies plus exfoliation of the epidermis (exfoliative dermatitis)

All the aforementioned histopathologic features are seen in cases of psoriasis and its atypical manifestations in which the history and clinical

¹⁸ Heimann W. I. Histopathology, *J. Cutan. Dis.* **34**:203 (March) 1916
 Histopathology of Lichens, Lichenifications and Neurodermatitis *ibid.* **35**:28 (Jan.) 1917

findings are beyond question diagnostically. The histopathologic changes vary with the type of lesion. The lesions vary according to the alteration in the balance of the various factors of resistance of the skin.

Weeping without vesiculation takes place by the exudation of serum from the dilated intercellular spaces, the flow of which meets no resistance by the parakeratotic scale. Therefore, when this flow is retarded by the increased resistance of the upper layer of the epiderm vesicles are formed in the area of least resistance.

The genesis of the vesicle depends on edema. The actual cause of edema is not known, but it seems to be due to a serotaxis in response to an irritant. There appears to be a difference of opinion among authorities as to whether edema is primarily intercellular or intracellular. Unna stated that it is intercellular, whereas Leloir expressed the opinion that it is intracellular, and Darier stated that both conditions occur together. Purely from a physical basis, the latter opinion would appear the most logical.

In eczema there is a more active exciting cause or an abnormal reaction producing spongiosis and vesiculation, whereas in psoriasis the exciting cause is less potent, and a slower, more stable, tissue reaction usually takes place, causing the same picture but ordinarily without spongiosis and vesiculation.

It appears that in all cases the area adjacent to the lesion is somewhat affected by the process. It is possible that when a heavy granular layer is present the eruption is limited to smaller areas because of an increased suprapapillary resistance, and an entirely different picture is produced.

There is no one feature of psoriasis that cannot be found in the other superficial inflammatory dermatoses. There is no absolute pathognomonic histopathologic criterion in psoriasis. However, when both the histologic and the clinical findings agree in the majority of details the condition should be classed with the superficial inflammatory dermatoses under the descriptive title psoriasis.

SUMMARY

A basic histopathologic formula is developed from a study of biopsy specimens taken from clinically typical psoriatic lesions of 50 patients.

The aberrant lesions are placed in convenient clinical groups, and a brief description of the histologic abnormalities is given.

The incidence of aberrant lesions in psoriatic patients is approximately 1 in 6.

A simple histologic classification of the aberrant lesions is given.

CONCLUSIONS

There were certain features of the study which were impressive enough to be recorded

1 Psoriasis cannot be unequivocally diagnosed from observations of a histologic section without considering the clinical findings

2 The aberrant lesions link psoriasis definitely as a fixed phase of a superficial dermatitis which may have the same etiologic factor as exfoliative dermatitis on the one hand or seborrheic dermatitis, eczema, neurodermatitis, etc., on the other

3 The histopathologic architecture tends to change in conformity with the evolution of the clinical lesion

Drs David L. Satenstein, Alexander Fraser and Frank Fraser assisted in the examination and interpretation of the histologic material

We present this report without offering a final conclusion. The subject is open for, and requires, further study. We hope that others may be encouraged toward a similar line of investigation. Eventually it may help to evolve a new and better concept of the pathogenesis of many cutaneous disorders.

ABSTRACT OF DISCUSSION

DR CLARK W. FINNERUD, Chicago. I believe that this study deals largely with the histopathologic and clinical variants of psoriasis, rather than with histogenesis. With regard to the histogenesis of the disease, the observations carried out by Dr. Ebert in our laboratory tend to support the theory stressed by Kyrle that psoriasis is primarily an epitheliosis and that it may be produced by a virus of some kind acting on favorable soil. In a case of acute psoriasis, histologically and clinically characteristic, a scratch mark was made, and forty-eight hours later a part of this was excised. Kyrle's acidophilic cytoplasmic inclusion bodies, similar to the Guarneri bodies of variola, were readily demonstrated. These were extruded from the nucleus and nucleolus into the cytoplasm. The initial and sole change at this time appeared to be in the epidermis. Control Kobner scratch marks gave negative results. The presence of psoriasis does not preclude the occurrence of other cutaneous diseases. Every one has seen other cutaneous involvements occurring in association with psoriatic disorders, some of which may somewhat resemble psoriasis. On the other hand, psoriasis may cause lesions of varying clinical and histologic character, resulting, among other factors, from the varying architecture of the skin in different parts of the body. It has been my experience that a disease which simulates another clinically also commonly tends to simulate it microscopically. For instance, one sometimes sees a patient with a clinical picture suggesting a questionable diagnosis of lupus erythematosus or lichen planus, and one finds that the lesions even simulate each other histologically, whereas ordinarily they do not. As stated by Dr. Foster, there are no pathognomonic histologic observations in psoriasis, although some occur more consistently than others. No one process exists in the lesions that does not occur at times in the lesions of certain other dermatoses. From the evidence presented, I cannot consider psoriasis as anything but a clinical entity. This disease, like syphilis, erythema multiforme, dermatitis venenata and various other diseases, is capable of producing various clinical and histologic pictures.

DR FRED WISE, New York There is a group of dermatologists, especially British, who regard psoriasis and seborrheic eczema as different manifestations of the same disease, which opinion has considerable bearing on this subject. If one regards psoriasis as a tissue reaction of the skin resulting from an insult or a combination of various provocative factors instead of from only one factor attacking the predisposed skin as a whole, one can conceive of at least a partial explanation for the occurrence of atypical and aberrant lesions in psoriasis. Every dermatologist frequently encounters patients with eruptions about the genitals and intergluteal regions which on cursory examination are diagnosed as seborrheic eczema, ringworm or ordinary intertrigo, only to have the eruption prove to be psoriasis after longer observation or careful examination. It is probable that several diversified factors play a rôle in the formation of atypical lesions. Among these may be diet, sweat, friction, the use and misuse of water and of topical remedies and variations in temperature and climate. I think that even deterioration of the patient's general health and his physical and emotional upsets might act as possible causes for the production of atypical lesions. These unorthodox lesions have been studied by Jadassohn, who gave them the name "psoriasoid." In a recent article Robert Bernhardt (*Arch f Dermat u Syph* **171** 322 [March 16] 1935) pointed out some of the differences between the lesions of Jadassohn's psoriasoid and those of typical psoriasis. In psoriasoid (1) chalky white scales do not appear on scratching, (2) on removal of the scale there is an absence of an epithelial membrane, the surface being smooth, glistening red and almost moist, (3) instead of punctate hemorrhage, punctate purpura appears, and (4) there is a punctate serous exudation in some of the aberrant lesions which does not occur in the scratched lesions of true psoriasis. This corresponds closely to the histologic appearances described by Dr MacKee and Dr Foster. Atypical clinical and histologic changes are encountered in many cutaneous diseases, among them syphilids, tuberculids, lichen planus, mycosis fungoides, various forms of lymphoblastoma, parapsoriasis, granuloma annulare and many other dermatoses.

DR. HERMANN FEIT, New York I have recently been especially interested in the many so-called aberrant types of psoriasis, and I have seen cases in which the lesions resembled syphilis, dermatitis herpetiformis and the like. On examination I found that some of the lesions, especially those in single patches, represented epithelioma and lymphoblastoma. Dr Foster said that one cannot make a definite histologic diagnosis of psoriasis. But one should make use of the method of Brocq, curettage of the scales layer by layer for about fourteen or fifteen layers, and then one would come to the famous pellicle of Buckley, who never found the condition in any other disease but psoriasis. I think that this method is too little used in making a definite diagnosis of psoriasis. Psoriasis is a cutaneous reaction, because there is nothing that cannot elicit an outbreak of psoriasis. Any mental or physical distress or any metabolic disturbance in a patient who has this peculiar type of condition will cause some psoriatic reaction. It would be better, perhaps, to call this atypical form of psoriasis psoriasiform dyskeratosis.

DR GEORGE C ANDREWS, New York This paper clearly shows that one has not the right to call clinically atypical lesions psoriasis unless the histology is definite. This does not mean that I take the view that there is no such thing as pustular psoriasis of the palms and soles. However, I object to including cases of pustular eruptions on the palms and soles in which there are clinical lesions of psoriasis and the histologic changes typical of psoriasis are not present and in which there is no suspicion of psoriasis in the personal or the family history.

Whether the aberrant lesions described in this paper should be classified as psoriasis is not of as much importance as the effort to determine the etiology of psoriasis. Dr Stokes recently spoke of an underlying cause and a precipitating cause in reference to rosacea. A similar conception applies to psoriasis and the aberrant lesions mentioned by Dr Foster and Dr MacKee. The predisposing condition in these cases is an underlying tendency to parakeratosis in some persons. This accounts not alone for the clinical features but also for similarities in the histologic observations in many of the sections studied by the authors.

DR DAVID BLOOM, New York. In 7 of 8 cases of pustular psoriasis the lesions presented the typical clinical features described in the literature by Barber and others. Specimens from 5 patients were examined microscopically. In 2 the typical histologic picture of psoriasis was present, and the pustules manifested themselves as a conglomeration of Monro abscesses situated between the corneous layer and the epithelial layer, in 1 case the histologic picture of psoriasis was present, with a large intradermal pustule, and in another case simple inflammation was seen. In the fifth case, in which the condition was diagnosed clinically as keratosis with the formation of pus, microscopic examination revealed typical psoriasis with the same intradermal pustule as was seen in 1 of the other cases. The clinical picture, the course, the extreme resistance to any treatment and the sterility on mycologic and bacteriologic examination make pustular psoriasis a disease entity. Its frequent association with typical psoriasis elsewhere on the body and the previously described histologic observations justify the name pustular psoriasis. The study of atypical lesions may give a clue to the etiology of this mysterious disease.

DR ADOLPH B. LOVEMAN, Louisville, Ky. Within the past year I carried out autogenous skin transplants in a case of psoriasis. These were grafts of full thickness, carried out with the patient under general anesthesia. I hope to repeat this experiment at the first opportunity. The results appear to coincide with those reported by Sulzberger and Wise in cases of eruptions caused by phenolphthalein. The psoriatic lesion transplanted to normal skin did not cause psoriasis, but I believe that the normal skin transplanted to the psoriatic patch did become psoriatic. By observing these grafts frequently I had an opportunity to study some of the other lesions and in doing so observed another similarity to certain types of drug exanthems, namely, that psoriasis apparently is a fixed eruption. The lesions seem to return in the identical location in which they previously existed. If this is true and if the experiment with autogenous skin transplants can be repeated and verified, I believe that I have evidence that psoriasis is a systemic disease manifesting itself on the skin as a result of a hematogenous spread.

DR MARION SULZBERGER, New York. This is probably the largest consecutive series of cases of typical and atypical psoriasis ever carefully investigated histologically. I have always been of the opinion that psoriasis is a more or less polymorphic disease, presenting many atypical lesions and in some instances an entire picture which is atypical. How many times does one find in a normal person in a nondermatologic group an eczematous patch, a patch of neurodermatitis or some other chance dermatologic finding? Does one find such an associated, but not necessarily connected, dermatosis in 1 of every 6 patients who present themselves to a gynecologist or to an ophthalmologist, or even in 1 of 6 patients with acne? If one includes such almost universal diseases as intertriginous ringworm, mild acne and pityriasis of the scalp, one will find such diseases in 1 of 6 normal controls. However, these are not exclusively the conditions to which the authors have alluded and one must come to the conclusion that there is some obligatory connection between the presence of at least some of the atypical lesions

and the psoriasis. What is the connection? One hypothesis is that these are psoriatic lesions altered for some unknown reason by the soil or by individual predisposition. That, I think, is manifestly true of a certain percentage of the lesions described. It is logical to assume that seborrheic dermatitis-like and intertriginous lesions are altered psoriatic lesions, although the histologic observations are atypical. There is another type of lesion described by the authors which is probably not an altered lesion of psoriasis, but which occurs in increased incidence in psoriatic patients. To explain this one must hypothesize that the patient with a tendency to psoriasis has a weakened integument, which has in some way increased his susceptibility to the other dermatosis. It would be easy to suppose that the psoriatic scale may be more permeable than the normal horny layer and may therefore allow the penetration of sensitizing substances. The scale may also form a culture medium for pathogenic or saprophytic organisms which multiply and thereby produce hypersensitivity to fungi and bacteria. I am inclined to believe that these two explanations are correct, that some of the concomitant lesions described by Dr Foster and Dr MacKee are altered psoriatic lesions and that some of them are supervening lesions of other dermatoses to which the psoriasis has in some way predisposed the patient. One must also consider the possibility of psoriasis supervening on the actual areas irritated by another dermatosis, or, vice versa, another dermatosis appears at the actual site of a psoriatic irritation, as in the isomorphic irritant phenomenon of Kobner.

DR PAUL D FOSTER, Los Angeles. That there are concomitant cutaneous conditions in psoriasis is true, but I believe that the high percentage of aberrant lesions found in patients with typical psoriasis, as shown by those with the five main types, that is, eczema, seborrheic dermatitis, neurodermatitis or chronic lichenified eczema, pustular psoriasis and erythematous squamous dermatitis, occur more frequently in patients with psoriasis than in the usual group of patients with cutaneous diseases or in any other given group of patients. Jadassohn did some excellent work on the psoriasoids, but I do not find a connection between his work and ours. It seems to me that the patients he studied had more atypical psoriasis, he studied the problem in patients with borderline differentiation, while we studied atypical lesions of patients with typical psoriasis. Dr Andrews said that one has no right to make a diagnosis of pustular psoriasis without lesions of psoriasis elsewhere. Dr MacKee and I are unable to support this contention. In 6 of the cases that we studied psoriasis was present on other parts of the body and in 3 it was not. In the 3 cases in which psoriasis was present the condition was classified as pustular psoriasis because of the typical picture presented in the histopathologic section plus the clinical details that have been emphasized by Barber, MacKee, Bloom and others. We believe that it is possible to diagnose the condition clinically in most cases of localized psoriasis on any part of the body, even on the nails alone. Typical pustular psoriasis of the palms and soles can be diagnosed clinically as such in the majority of cases by those who have had experience, regardless of the lesions on the rest of the body. In pustular psoriasis the formation of the pustules is a simple matter. Dermatologists are familiar with the formation of the Monro-Sabouraud abscesses, the tunneling, the insinuation of the leukocytic cells into the epiderm and the exocytosis and exoserosis into and through the epithelium beneath the corneous layer, and in most cases of psoriasis, that is, in the typical lesions, the parakeratotic layer and the corneous layer are loose enough to allow these cells to be desquamated with the scale. On the palms and soles is a thick hyperkeratotic layer, a barrier holding down the excretion of these substances so that beneath the hyperkeratotic layer is a collection of the leukocytes and the degenerated epithelial cells to form the lakes of pus, giving a different clinical picture. Dr Loveman's observation opens new channels for investigation.

ANTISYPHILITIC TREATMENT

EFFECT OF REST ON THE RESULTS OF TREATMENT AND THE GENERAL BENEFIT DERIVED FROM THERAPY

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AND

S WILLIAM BECKER, M D

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The problem expressed in the title of this paper has been given little consideration in modern syphilologic literature. Among the modern textbooks only that by Stokes¹ gives adequate consideration to a discussion of the paramount necessity of rest as an adjunct to specific treatment, while others have little or nothing to say. Even less can be found about the general effect of specific treatment on the patient. Yet the distinct influence which antisyphilitic treatment has on the patient's general well-being must be apparent to every experienced syphilologist. To a certain extent this influence can be objectively evaluated, for example, by the increase in the patient's weight. There is, however, a less tangible, but none-the-less important, change which can be observed in the majority of the patients, namely, a distinct improvement in the subjective feeling of well-being. In cases of latent syphilis the difference between the way the patient feels before treatment has been given and his condition after it has been administered for some time has been so especially striking that we thought it advisable to give this problem further consideration. The object of our endeavor was to evaluate the various factors which might be responsible for both subjective and objective improvement in the majority of our patients and for lack of improvement in the minority.

The general beneficial effect of antisyphilitic treatment is caused by the following factors

1 *The specific effect of antisyphilitic drugs* This needs no explanation. It is readily understood that elimination (in toto or in part) of a chronic infectious process will result in an improvement of the general well-being of the patient.

This work was aided by funds from the A. B. Kuppenheimer Foundation.

From the Section of Dermatology of the Department of Medicine, University of Chicago. Read at the Scientific Session of the Section of Dermatology, June 7, 1935.

1 Stokes, John H. *Modern Clinical Syphilology*, ed. 2, Philadelphia, W. B. Saunders Company, 1934.

2 *The nonspecific effect of antisyphilitic drugs* This seems to play a negligible rôle as far as compounds of mercury and bismuth are concerned but is a definite factor in the case of the arsenical compounds. The arsphenamines are of distinct value against a number of non-spirochetal conditions, e g, tuberculosis of the skin, blastomycosis and multiple sclerosis. Their tonic action—undoubtedly due to their arsenic content—form a welcome addition to the effect of treatment. This tonic action is most pronounced in patients treated with tryparsamide, in whom considerable gain in weight is to be expected. In addition, tryparsamide is a mild aphrodisiac, most welcome in raising the spirit of the discouraged and depressed tabetic patient.

3 *The effect of nonspecific treatment* It has been realized for a long time that it is a serious mistake to treat syphilis merely chemically. Syphilis shows many parallels with tuberculosis, so close that even microscopic examination sometimes cannot differentiate the clinical manifestations of the two diseases, the continuous fight between the defense mechanism of the host and the virulence of the etiologic agent is common to both. It is now definitely recognized that resistance-building measures, especially rest, are necessary in the treatment of tuberculosis. This is just as important in the treatment of syphilis, in which the results of poor therapy are more remote and not as dramatic as in tuberculosis. During the prearsphenamine era this was well understood by the syphilologists, vacations at spas, hot water, steam and sulfur baths and stimulation via the gastro-intestinal tract (with a compound decoction of sarsaparilla) were in general use. Primitive people (African Negroes in Assuan) have been treating syphilis with symptomatic success by burying the patient for several days in hot desert sand and administering decoctions.

With the advent of the arsphenamine era all the empirical achievements of additional nonspecific treatment of syphilis were momentarily forgotten. The overwhelming "chemical success" ruled the development of methods of treatment. Yet, as has occurred in the practice of medicine throughout the ages, the pendulum was bound to swing back. During the past decade extensive research, both on human beings and on animals, has put the empirical knowledge of nonspecific treatment on a more scientific basis. The tissues react against the invasion by *Spirochaeta pallida* by a process termed *Umstimmung* (Pirquet). This resistance phenomenon represents, teleologically speaking, the curative endeavor of the organism (Bloch). We are able to bring about an important increase in this mechanism of defense by nonspecific

physical or chemical therapy The work of Rajka and Radnai ² and of Gottron ³ shows that systemic ultraviolet irradiation has a distinct influence on the involution of syphilitic lesions In combination with autohemic injections, resistant syphilis, including the so-called serologically fast syphilis, has been successfully treated The course of experimental syphilis in rabbits has been materially influenced by sunlight (Brown and Pierce) ⁴ Stimulation of the esophylactic properties of the skin was successfully tried in the form of experimentalunctions with ointments not containing mercury by Jarisch,⁵ Salomon and Hubner, and Hoffmann ⁶ The results did not differ materially from those following ordinary mercurialunctions The beneficial effect of the treatment of syphilitic patients in spas has been found to be due to a combination of several factors In some of the spas the direct action of heat (hot springs) and perspiration must be considered This is in accord with the results of experiments with rabbits by Weichbrodt and Jahnel,⁷ Schamberg and Rule ⁸ and Frazier,⁹ who observed the more rapid disappearance of syphilitic lesions of all stages after treatment with hyperpyrexia than after the use of mercury Other factors are rest, change of climate, stimulation of metabolism and stimulation of the skin as an organ, presumably causing a beneficial reaction on the sympathetic nervous system Here we may also mention that gymnastics, massage and outdoor exercise are of recognized value in the treatment of tabes It is not within the scope of our study to go into the wide and successful aspects of the various methods of therapy with non-

2 Rajka, E, and Radnai, E Ueber die gunstige Beeinflussung der Wa R und Neurosyphilis mit Licht-, beziehungsweise mit kombinierter Licht- und Eigenblutbehandlung, *Compt rend Cong internat de dermat et syph*, 1931, p 995

3 Gottron, H, in discussion on Rajka and Radnai ²

4 Brown, Wade H, and Pierce, Louise The Influence of Light on the Reaction to Infection in Experimental Syphilis, *J Exper Med* **45** 497 (March) 1927

5 Jarisch Therapeutische Versuche bei Syphilis, *Wien med Wchnschr* **45** 721, 1895

6 Quoted by Jadassohn, J Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol 18

7 Weichbrodt and Jahnel Einfluss hoher Temperaturen auf Spirochaeten und Erscheinungen der Lues im Tierversiment, *Deutsche med Wchnschr* **45** 483, 1919

8 Schamberg, Jay Frank, and Rule, Anna M Therapeutic Effect of Hot Baths in Experimental Primary Syphilis in Rabbits, *J A M A* **88**.1217 (April 16) 1927

9 Frazier, Chester N Effect of Elevation of Body Temperature on the Course of Experimental Syphilis in the Rabbit, *Arch Dermat & Syph* **16**.445 (Oct) 1927

specific protein and with fever We wish to mention, however, that we have also found the combination of generalized ultraviolet irradiation and injections of autogenous blood a valuable aid in converting persons with a tendency to relapse into normally reacting patients

4 *The patient's habits and ways of living*—Any one afflicted with a constitutional chronic infectious disease should live according to a certain regimen if he expects the full benefit of medical treatment Patients with syphilis are no exception to this Stokes¹ said "Rest is one of the potent, and often life-saving factors in the general management of the syphilitic patient More and more frequently in the recent literature one encounters the theory that loss of resistance to the disease and failure to make therapeutic headway against it are functions of the exhaustion of the defence mechanism, including presumably the reticulo-endothelial system and the antibody-forming agencies, a loss of function which may be recovered after rest" Normal sleeping hours, a nap after luncheon, reduction of mental and emotional strain and regular vacations, spent preferably in the country, are essential additions to the specific treatment The diet presents another point of attention Since constitutional syphilis is associated with marked consumption of proteins, the diet of the patient should be rich in calories and especially in proteins

Thus far we have been better aware of the deleterious consequences which follow the breaking of the outlined rules than of the beneficial effects if they are conscientiously obeyed For instance, it is known that the victims of dementia paralytica are frequently high-strung business men of the "neurocirculatory instability" type described by Becker¹⁰ The onset of tabes often follows periods of stress The peripatetic patient (Moore¹¹) of the traveling salesman type has a poor prognosis because of the absence of a regulated life Heavy physical exertion predisposes to aneurysm The indiscriminate use of alcohol has long been known to delay progress and to produce relapse Excessive use of tobacco predisposes to leukoplakia All in all, the bad effect of wear and tear is too definite to be doubted

It should not pass unmentioned, however, that the striking improvement in the feeling of general well-being, as brought on by the various

10 Becker, S W Dermatoses Associated with Neuro-Circulatory Instability Generalized and Localized Pruritus, Neurodermatitis, Dyshidrosis, Urticaria and Angioneurotic Edema, Lichen Planus, Neurotic Excoriations, Alopecia Areata, Dermatitis Herpetiformis and Scleroderma, Arch Dermat & Syph 25 655 (April) 1932

11 Moore, Joseph Earle The Modern Treatment of Syphilis, Springfield, Ill, Charles C Thomas Publisher, 1933

factors which we have discussed, may sometimes be a drawback. In fact, the patient who experiences the general benefit of the treatment is frequently only too likely to minimize the danger of the disease and to consider himself cured at a time when he is going through the most critical period of his infection.

INVESTIGATIONS

Our study was carried out by supplying each patient with the questionnaire shown in table 1. The lower portion was filled out by the patient, and data for the upper portion were obtained from the patient's record.

TABLE 1—*Questionnaire*

Name	Date
Sex	Age
Weight before treatment	Unit No
Weight at present time or one year after beginning of treatment	
Diagnosis	
Serologic peculiarities	
(e. g. Wassermann fast, persistently + spinal fluid, serologic relapses)	
Clinical symptoms due to syphilis	
(e. g. gastric crises, impairment of vision)	
We would appreciate it if you would answer the following questions	
What kind of work do you do?	
How many hours daily?	How many days weekly?
Do you take a vacation every year?	How many weeks?
How do you spend your vacation?	
How do you spend your week ends?	
Do you take any form of exercise?	
Do you keep regular sleeping hours?	How many hours?
Do you take a nap after luncheon?	
How did you feel before treatment was started?	
Do you feel differently now?	
How long did you take treatment before you noticed this change?	
How do you feel now?	

Questionnaires were sent to 500 patients chosen at random, who were of all ages and in all stages of syphilis and who had been treated for at least one year. Answers were received from about one half of this number. Several questionnaires had been filled in in such a way as to make correct evaluation impossible. After these were discarded, 236 answers remained, on which this study is based. Since our institution is a pay clinic, the patients were in general of a higher type than can be found at the free dispensaries. The social stratum may be said to correspond with that of the patients of the city practitioner.

The questionnaires were separated into three groups according to the statements made by the patients:

Feeling of general well being improved	171	72 per cent	Group I
Feeling of general well being not improved	73	22 per cent	Group II
Feeling of general well being impaired	12	5 per cent	Group III

In order to study the influence of the patients' habits and ways of living, the patients of each group were classified into one of three classes

1 Regular and relaxed Only such patients were included as stated that their working hours were not longer than nine hours per day, that their sleeping hours were regular and not less than eight hours and that they took a vacation every year

2 Moderately resting Patients in this class had stated that their working hours were not longer than nine hours per day, that their sleeping hours were regular and not less than eight hours but that they took no vacation or that they had less than eight but not less than seven hours of sleep and took a yearly vacation

3 Nonresting Patients in this class stated that they either had abnormally long working hours, kept irregular sleeping hours or had six hours or less of regular sleep and, for the most part, took no vacation

For simplification we shall refer to these classes as rest plus, rest normal and rest minus Our three groups of patients were thus analyzed as table 2 shows

The information given in table 2 is obvious The patient who has had a better regulated life has obtained the best symptomatic improve-

TABLE 2—*Number and Percentage of Patients from Each Group*

Group	Rest +		Rest N		Rest —	
	No	Percent age	No	Percent age	No	Percent age
I	42	25	79	46	50	29
II	11	20	11	20	31	60
III	3	25			9	75

ment This effect becomes even more apparent if the results are analyzed according to the clinical form of syphilis treated Thus it was found that of the rest plus patients of group III, one had dementia paralytica, one suffered from late vascular syphilis and chronic degenerative arthritis and one was Wassermann-fast, with involvement of the central nervous system This explains the lack of improvement in the rest plus patients in group III

These experiences are in line with the observations of one of us (S W B) that the results of treatment at the Mayo Clinic, where the patients are hospitalized for one day after the administration of arsphenamine and rest during the remainder of the week, are better than the results obtained in urban practice, in which the patients are working and cannot be hospitalized A physician working in a marine hospital stated that the best therapeutic results he had ever seen were in hospitalized syphilitic patients

In table 3 is shown the ratio of the percentage of patients who gained to that of patients who lost weight It can be readily seen from this that the ratio between the percentage of patients who gained and the

percentage who lost weight is favorable to the former in the rest plus and rest normal patients of groups I and II, while it reverses sharply in the rest minus patients (The loss of weight in 100 per cent of the patients of group III is easily explained by the aforementioned forms of disease in the rest plus patients of this group)

We gained through this study an insight into the habits and ways of living of the average American in Chicago, and the most striking fact gathered seemed to us the scarcity of regular yearly vacations (Only 38 per cent of our patients took vacations. Moreover, the average vacation is one or two weeks, a time insufficient for full relaxation, even if the time is spent as it should be, in a lake cottage or on a fishing trip. But, alas, the majority of the patients stated that they spent their week-ends and vacations touring or visiting with friends!)

TABLE 3—*Ratio of Percentage of Patients Who Gained to That of Patients Who Lost Weight*

Group	Class	Percentage Who	
		Gained	Lost
I	rest +	66	34
	rest N	64	33
	rest —	46	52
II	rest +	77	13
	rest N	66	34
	rest —	26	74
III	rest +	0	100
	rest N		
	rest —	0	100

CONCLUSIONS

The data gained from this study show sufficient beneficial effect of regular and restful living to warrant the statement that the physician who treats syphilis should emphasize to every patient under his care the paramount necessity of rest and relaxation for obtaining the most satisfactory results from antisyphilitic treatment. Failure to observe regular hours of rest and to take vacations leads to poorer results from therapy. Life in the large cities has led to overactivity and frustration of the human need for emotional and physical relaxation. Reeducation to a more restful way of living should be part of the task of physicians.

SUMMARY

The factors which lead to the general beneficial effect of antisyphilitic treatment are discussed. The seemingly forgotten effect of non-specific treatment is stressed on the ground of the striking parallels

between syphilitic and tuberculous infection. The value of generalized ultraviolet irradiation and of autohemic injections in certain cases of resistant syphilis is confirmed.

The study deals with the influence of the patient's habits and ways of living on the general beneficial effect derived from therapy. Data compiled by means of questionnaires, analyzed and given in tables, reveal the paramount beneficial influence of restful living on the subjective feeling of well-being as well as on increase of weight on the part of syphilitic patients.

Physicians who treat syphilis should not treat the patient merely specifically but should utilize the value of decreased tension of the patient's life.

LYMPHOGRANULOMA INGUINALE

III THE USE OF LYMPHOGRANULOMATOUS MOUSE BRAINS FOR DIAGNOSIS

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AND

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In previous communications¹ we have described the isolation of the virus of lymphogranuloma inguinale from the pus and glandular tissue of a patient with the inguinal type of the disease and its successive transmission through white mice. We have also found, confirming Wassen's² observations, that lymphogranulomatous mouse brains offer an excellent source of highly potent and specific antigen for the performance of the Frei test. This work has been repeated recently by Lichtenstein and von Haam³.

The purpose of the present paper is to record the results of one year's clinical use of antigen prepared from mouse brain for the diagnosis of lymphogranuloma inguinale. Prior to the introduction of material from experimental animals the only antigen available was that prepared from pus from a human being, as first described by Frei⁴. This original antigen consisted of an emulsion in a physiologic solution of sodium chloride of pus taken from a suppurating gland of a patient with the inguinal type of the disease and heated to destroy the etiologic agent present.

From the New York Hospital and the Department of Medicine, Cornell University Medical College

1 Grace, A W, and Suskin' F H (a) Successive Transmission of Virus of Lymphogranuloma Inguinale through White Mice, *Proc Soc Exper Biol & Med* **32** 71 (Oct) 1934, (b) Lymphogranuloma Inguinale II The Cultivation of the Virus in Mice and Its Use in the Preparation of Frei Antigen, *Arch Dermat & Syph* **33** 853 (May) 1936

2 Wassen, E Receptivite de la souris blanche a l'egard du virus lymphogranulomateux (maladie de Nicolas et Favre), *Compt rend Soc de biol* **114** 493, 1933

3 Lichtenstein, L, and von Haam, E Usefulness of Organ Emulsions of Infected Animals in Diagnosis of Lymphogranuloma Inguinale, *Proc Soc Exper Biol & Med* **32** 952 (March) 1935

4 Frei W Eine neue Hautreaktion bei Lymphogranuloma inguinale, *Klin Wochenschr* **4** 2148 (Nov 5) 1925

The use of pus from a human subject for the preparation of antigen has several drawbacks, namely

1 Patients with the inguinal type of lymphogranuloma inguinale in a suppurative stage are not encountered often and can be used as a source of antigen only if the pus is uncontaminated with other organisms. Secondary infection following sinus formation occurs frequently enough to make suitable pus scarce.

2 It is difficult to be certain that pus from inguinal glands is free from the causative agents of other venereal diseases. This applies especially to chancroid, the etiologic agent of which (Ducrey's bacillus) is sometimes found in inguinal pus but is relatively difficult to demonstrate in direct smears or by growth on artificial mediums. The Ito-Reenstierna test with a stabilized vaccine of Ducrey's bacillus enables the determination of a past or present chancroid infection to be made with certainty, but the vaccine required is not readily available.⁴¹

3 When a patient from whom suitable pus may be obtained presents himself, the pus is usually available only in small quantities. Only on rare occasions have we been able to aspirate more than from 3 to 5 cc at one time.

4 Specimens of pus taken from different patients with lymphogranuloma inguinale vary in antigen content.⁵ This variation may be so marked that an antigen prepared from a 1:10 dilution of one sample of pus may evoke a strongly positive reaction in a lymphogranulomatous person whereas one made from a 1:5 dilution of pus from another patient may elicit a much weaker reaction in the same subject.

In May 1934, antigen prepared from lymphogranulomatous mouse brain was used for the first time at the New York Hospital for the performance of Frei tests. After a thorough trial of its potency and specificity as compared with antigen prepared from pus from a human being, it has now entirely replaced the latter in the diagnosis of lymphogranuloma inguinale at the New York Hospital.

The clinical conditions which are regarded as manifestations of lymphogranuloma inguinale and which therefore call for the performance of the Frei test are

4a The vaccine used for this test is known as Dmelcos vaccine and is manufactured in France. There is no evidence that the United States Treasury Department has licensed the importation and sale of this vaccine in the United States.

5 (a) Grace, A. W. Lymphogranuloma Inguinale. I. Preservation of Frei Antigen by Drying, Its Concentration in Fresh and Dried Pus, *Arch Dermat & Syph* **30** 823 (Dec) 1934. (b) Saenz, B. An Unusual Form of Allergic Cutaneous Reactions in Lymphogranulomatosis Inguinalis, *Arch Dermat & Syph* **31** 348 (March) 1935.

1 Acute and chronic inguinal adenitis, suppurative or nonsuppurative, in which no other etiologic agent (*Gonococcus* Ducrey's bacillus, *Spirochaeta pallida*, *Bacillus tuberculosis*, *Bacillus tularensis* or a simple pyogenic organism) or condition (Hodgkin's disease or neoplasm) can be found. These conditions represent the inguinal type of the disease, which has been described in detail by Durand, Nicolas and Favre,⁶ Hellerstrom,⁷ DeWolf and Van Cleve,⁸ Cole,⁹ and many others. It is enough to say here that the untreated condition is chronic and that indolent suppuration of the inguinal glands, sometimes preceded by an evanescent lesion of the genitalia and attended by the formation of multiple sinuses and a violaceous tint of the surrounding skin, should be regarded as suspicious of lymphogranuloma inguinale.

Since mixed venereal infections often occur, it is sometimes advisable to perform a Frei test even if etiologic agents other than that of lymphogranuloma inguinale can be demonstrated in association with inguinal adenitis. This is especially true in instances in which the picture of the bubo is atypical from either a clinical or a pathologic aspect.

2 Acute and chronic inflammatory disease of the anus, rectum and sigmoid colon, which may be accompanied by fistula in ano, rectovaginal fistula, abscesses or sinuses in the buttocks or stricture of the rectum. The condition is independent of the presence or absence of syphilis and gonorrhea. It is referred to as the anorectal type of lymphogranuloma inguinale. Good clinical descriptions of this condition, including etiology, have been given recently by Cole,⁹ Bloom,¹⁰ Wien and Perlstein¹¹ and Wien, Perlstein and Neiman.¹²

The commonest symptoms are the passage of blood and pus from the rectum and painful and difficult defecation. Externally, erythema, edema and tenderness of the perianal region or perianal warty excrescences may be found. In most of our patients, however, external lesions

6 Durand, M., Nicolas, J., and Favre, M. Lymphogranulomatose inguinale subaiguë d'origine gentale probable, peut-être vénérienne, Bull et mem Soc med d hôp de Paris **35** 274, 1913.

7 Hellerstrom, S. A Contribution to the Knowledge of Lymphogranuloma Inguinale, Acta dermat-venereol, supp 1, 1929, p 5.

8 DeWolf, H. F., and Van Cleve, J. V. Lymphogranuloma Inguinale, J. A. M. A **99** 1065 (Sept 24) 1932.

9 Cole, H. N. Lymphogranuloma Inguinale, the Fourth Venereal Disease Its Relation to Stricture of the Rectum, J. A. M. A **101** 1069 (Sept 30) 1933.

10 Bloom, David. Stricture of the Rectum Due to Lymphogranuloma Inguinale, Surg Gynec & Obst **58** 827 (May) 1934.

11 Wien, M. S., and Perlstein, M. O. Lymphogranuloma Inguinale, M. Rec **139** 288 1934.

12 Wien, M. S., Perlstein, M. O., and Neiman, B. H. Inguinal Lymphogranuloma in Its Relation to Stricture of the Rectum Arch Path **19** 331 (March) 1935.

were rare. Proctoscopic examination may reveal the rectal mucosa to be acutely inflamed and edematous, diffusely and irregularly scarred and ulcerated or converted into a firm, rigid tube. When edema, inflammation or ulceration is present, small nodular elevations of the mucosa are frequent, when it is acute, blood and pus often can be seen passing down the rectum. All degrees of narrowing of the rectal lumen are encountered, varying from that due to edema in the acute condition to a complete stenosis due to fibrosis when the involvement is of long standing. The vast majority of strictures occur between 2 and 6 cm above the anus, but sometimes they are found as high as 10 cm. Fistulas, with passage of material from the bowel through the vagina or the tissues of the buttocks or thighs, occasionally occur. Pyrexia, as a rule, is not a feature, but instances are occasionally met with in which there is a daily remittent fever, which may last for weeks. Inguinal lymphadenopathy is usually confined to a few shotlike glands. The pathologic picture of anorectal lymphogranuloma inguinale has been given by Barthels and Biberstein¹³ and more recently by Wien, Perlstein and Neiman¹². It is sufficient to state here that the normal tissue of the rectal wall is replaced in the early stages by an unusual type of granulation tissue and in the later stages by hyalinized fibrous tissue. It is this formation of fibrous tissue which is responsible for the resistance of the rectal lesions to therapy in the later stages of the disease. In the early stages the anorectal type of lymphogranuloma inguinale is benefited by the use of antimonial preparations, such as antimony and potassium tartrate, fuadin and stibamine glucoside. Our own cases, as well as those of Hebb,¹⁴ attest this. Investigation of the efficacy of Frei antigen in the treatment of anorectal lymphogranuloma inguinale is now in progress.

Lymphogranuloma inguinale of the anorectal type is said to be most prevalent among women, especially Negroes, and it is probable that most instances of inflammatory rectal stricture in Negro women are due to this disease. It must not be overlooked, however, that similar instances occur in white persons, men as well as women. In the department of dermatology of the New York Hospital, of which the clientele is predominantly white, nine white men and four white women are receiving treatment for this condition at the time of writing.

3 Chronic elephantiasis and ulceration of the vulva (esthiomene). Only one case of this condition has been encountered at the New York Hospital, an adequate description, therefore, cannot be given. Stannus,¹⁵

13 Barthels, C, and Biberstein, H. Zur Aetiologie der entzündlichen Rektumstrikturen, Beitr z klin Chir 152 161, 325 and 464, 1931.

14 Hebb, Arthur. Personal communication to the authors.

15 Stannus, Hugh S. A Sixth Venereal Disease, London, Bailliere, Tindall & Co., 1933, p 125.

in his excellent review on lymphogranuloma inguinale, summarized the symptomatology of esthiomene in the words of Koch ¹⁶

The labia majora were the seat of more or less marked thickening, with ulceration, occasionally with angiectatic erosions, rather less commonly the labia minora and clitoris were affected, the latter having often a "stalked" appearance, the skin had a bluish-red color and was ulcerated, sometimes also the mons, the commissure and peri-anal region were involved in the infiltrative process. The epithelium of the nymphae was in some cases smooth and macerated, in others the lips presented a verrucose, tuberoso or papillomatous appearance. There was a diffuse sclerotic condition of the mucous membrane about the openings of the urethra and vagina, in some cases leading to definite stricture. Ulceration might occur in any part of these infiltrated tissues, but was most common at the commissure, the opening of the urethra, on the inner surface of the labia minora and clitoris. Perforation might occur of the nymphae, at the fourchette or of the urethrovaginal and rectovaginal walls, with the formation of fistulas, or there might be greater destruction of tissues with the production of a cloaca, limited by portions of infiltrated skin and mucous membranes, rectovesical fistula might also be produced.

Esthiomene and the anorectal conditions previously mentioned constitute the genito-anorectal syndrome described by Jersild ¹⁷ and shown to yield a positive Frei reaction by Frei and Koppel ¹⁸

4 Elephantiasis of the male genitalia. This condition has not yet been encountered at the New York Hospital. Barthels and Biberstein ¹³ cited the report of a case of elephantiasis of the penis and scrotum occurring nine years after complete extirpation of an involved inguinal gland, which was associated with a typical primary lymphogranulomatous penile lesion. The male genitalia may also show a clinical condition similar to esthiomene in the female.

METHODS AND MATERIALS

The Technique of the Frei Test—The Frei test, as originally described by Frei,⁴ consists of the inoculation into the skin of the flexor surface of the arm of 0.1 cc of antigen prepared from pus from a lymphogranulomatous inguinal gland diluted 1:10 in a physiologic solution of sodium chloride and heated at 60 C for two hours on one day and at the same temperature for one hour the next day. Frei discovered that at the end of from forty-eight to seventy-two hours, in a person who has, or has had, lymphogranuloma inguinale, there develops at the site of the injection a bright red papule from 7 to 10 mm in diameter, whereas a nonlymphogranulomatous subject shows practically no reaction.

16 Koch, F. *Ulcus vulvae chronicum elephantiasicum*, Arch f Dermat u Syph 34:205, 1896.

17 Jersild, O. *Contribution à l'étude de la pathogenie du soi-disant syphilome ano-rectal* (Fournier), Ann de dermat et syph 1:62, 1920.

18 Frei, W. and Koppel, A. *Ulcus vulvae chronicum elephantiasicum (esthiomene) und sogenanntes syphilôme anorectal als Folgeerscheinungen und der Lymphogranulomatosis inguinalis*, Klin Wchnschr 7:2331, 1928.

The Use of Lymphogranulomatous Mouse Brains in the Frei Test—The antigens prepared from mouse brains which were employed in this work were prepared as follows. A mouse dying as a result of a previous intracerebral inoculation with the virus of lymphogranuloma inguinale was killed, and its brain was removed aseptically. The brain was emulsified in a sterile mortar with sterile physiologic solution of sodium chloride, and the emulsion was sealed in glass ampules and heated according to the method of Frei. The increase in virulence of the virus with successive passages in mice and a concurrent increase in the antigen content of mouse brains made it necessary to increase at intervals the dilution of the antigen. Thus, antigens prepared from the brains of mice used for the first to the eleventh passage consisted of a 40 per cent emulsion of mouse brain, those prepared from the brains of mice used for the twelfth to the twenty-third passage consisted of a 20 per cent emulsion, and those prepared from the brains of mice used for the twenty-fourth and subsequent passages consisted of a 10 per cent emulsion, the addition of 0.4 per cent of phenol to the emulsion produced no apparent alteration in its antigenic properties. The antigens were tested for bacterial contamination by aerobic and anaerobic culture before and after heating. Any material that showed bacterial contamination in forty-eight hours was discarded. After heating they were transferred to small vials capped with no-air rubber stoppers and were placed in the refrigerator until used. All antigens were tested within one month after preparation, and several were tested after standing for various lengths of time. It was also found possible to preserve lymphogranulomatous mouse brains by drying them in vacuo from the frozen state according to a method described in a previous communication⁵¹ and employing that dried material for the production of Frei antigen.

As the antigens increased in potency, it was not only sufficient to increase the dilution but was also necessary to decrease the dose administered for the Frei test. The volume of intradermal inoculum was maintained at 0.1 cc for antigens prepared from the brains of mice used for the first eleven passages, after which 0.05 cc was constantly used. To eliminate the possibility of mistaking a pseudo-reaction produced by the protein of the mouse brain for a positive Frei reaction, control tests were made concurrently with an emulsion of normal mouse brain prepared and used in the same manner as the antigen prepared from lymphogranulomatous mouse brain.

Subjects Used for the Performance of the Frei Test with Antigens Prepared from Mouse Brains—The series of subjects tested included twenty-seven lymphogranulomatous and thirty-eight nonlymphogranulomatous persons.

Lymphogranulomatous Subjects The series of lymphogranulomatous patients was made up of two groups: (1) those who presented the inguinal type of the disease and (2) those who showed the anorectal type.

The patients with the inguinal type consisted of twelve men, eleven white and one Negro. Four of them were tested during the active stage of the disease, and the remaining eight, who included the Negro, had healed lesions. Five of the latter had been treated at the New York Hospital within the last two years for purulent inguinal adenitis due to lymphogranuloma inguinale. The three other men had acquired their infections eight, eighteen and twenty years before, respectively, and the condition was recognized by old inguinal scars.

The patients with the anorectal type comprised seven white men and eight women, three white and five Negro. The fifteen patients presented the following lesions: Three patients had acute proctitis, one with an accompanying pyrexia, eight had subacute proctitis with partial rectal stricture, and four had complete stenosis of the rectum, for which colostomy had been performed. The cause of

the rectal condition in three of the patients with colostomy was unknown at the time of operation, which took place from several months to five years prior to admission to the department of dermatology of the New York Hospital. The pathologic report of examination of a portion of the rectal wall removed from one of the women (who also had rectovaginal fistulas) revealed chronically inflamed granulation tissue, with a number of minute round faintly acidophilic bodies, intracellular and extracellular, especially in the more necrotic portions. These bodies closely resembled the intracytoplasmic bodies encountered in lymphogranulomatous inguinal buboes¹⁹ and in the brains of mice which died from infection with the virus of lymphogranuloma inguinale²⁰.

Five persons from group 1 and seven from group 2 were syphilitic. Of these twelve patients, three had neurosyphilis, one had a perforated nasal septum and eight had only a positive Wassermann reaction or a history of syphilis.

Nonlymphogranulomatous Subjects. The thirty-eight nonlymphogranulomatous subjects were divided into four groups (groups 3, 4, 5 and 6) as follows:

Group 3 was made up of seven patients who showed inflammatory inguinal adenitis at the time of Frei testing. Four of them had chancroid, as determined by a positive reaction to the Ito-Reenstierna test, two had staphylococcal abscesses and one had primary syphilis. Two members of this group also had latent syphilis.

In group 4 there were four persons with rectal disease. Of these, one had primary rectal syphilis with inguinal buboes and three had neoplasms.

Group 5 consisted of twenty-two inpatients of the general medical and surgical services who had no history of inguinal lymphadenopathy, rectal disease or syphilis.

In group 6 there were seven persons with syphilis, three of whom were also in groups 3 and 4. Of the four not mentioned heretofore, one had dementia paralytica, another had tabes and two had the disease in a latent form.

Owing to the large number of antigens tested, eighty-eight in all, in addition to the control material, and to the limited number of subjects available, each person was given repeated inoculations at intervals, at least two antigens being given at one time. Duplicate and triplicate tests in different lymphogranulomatous and nonlymphogranulomatous subjects were made as often as possible with each antigen. In this way, 150 tests were performed in the twenty-seven lymphogranulomatous subjects and 143 in the thirty-eight nonlymphogranulomatous ones.

RESULTS

Reaction to Inoculation with Antigen Prepared from Mouse Brain.—The results obtained by the use of lymphogranulomatous mouse brains for the diagnosis of lymphogranuloma inguinale are set forth in table 1. The antigens employed were prepared from the brains of mice used for the second to the forty-fourth passage of the virus and were prepared and administered according to the methods given in the preceding section.

It will be noted that in compiling the table only the size of the central papule was recorded and no mention was made of the surrounding erythematous zone which usually was present at the end of from forty-eight to seventy-two hours,

19 Favre M. Sur l'etiologie de la lymphogranulomatose inguinale subaiguë (ulcère vénérien adénogène). *Presse med* 32 651 1924.

20 Findlay, G. M. Experiments on the Transmission of the Virus of Climatic Bubo (Lymphogranuloma Inguinale) to Animals. *Tr. Roy. Soc. Trop. Med. & Hyg.* 27 35 (June) 1933. Grace and Suskind^{1b}.

especially in positive reactions. The reason for the omission is that the size of the papule was the most constant element of the reaction and the size of the surrounding flare varied considerably. Erythema was seldom observed in negative reactions.

TABLE 1—*Reactions of Various Groups of Subjects to Tests with Frei Antigen Prepared from Lymphogranulomatous Mouse Brain and with Emulsion of Normal Mouse Brain*

Material Used in Intradermal Test	Lymphogranulomatous Persons			Nonlymphogranulomatous Persons		
	Average Size of Papule, Mm	Number of Persons Tested	Number of Tests	Average Size of Papule, Mm	Number of Persons Tested	Number of Tests
(1) All Lymphogranulomatous and Nonlymphogranulomatous Persons						
Lymphogranulomatous mouse brain	8.7	27	95	2.7	38	105
Normal mouse brain	2.2	27	55	2.0	38	38
(2) Persons with Active Inflammatory Inguinal Adenitis						
Lymphogranulomatous mouse brain	9.0	4	17	3.0	7	19
Normal mouse brain	2.1	4	7	2.3	7	12
(3) Persons with Old Healed Inguinal Lymphogranuloma Inguinale						
Lymphogranulomatous mouse brain	9.2	8	28			
Normal mouse brain	2.6	8	9			
(4) Persons with Rectal Diseases						
Lymphogranulomatous mouse brain	8.2	15	50	2.6	4	9
Normal mouse brain	2.2	15	20	2.1	4	4
(5) Persons with Syphilis						
Lymphogranulomatous mouse brain	8.9	12	48	2.5	7	12
Normal mouse brain	3.1	12	19	1.8	7	8
(6) Nonlymphogranulomatous Persons Without Inguinal or Rectal Disease or Syphilis						
Lymphogranulomatous mouse brain				2.4	22	56
Normal mouse brain				1.6	22	22

An analysis of table 1 follows.

All Lymphogranulomatous and Nonlymphogranulomatous Persons. The great difference in reaction to antigen prepared from lymphogranulomatous mouse brain between lymphogranulomatous and nonlymphogranulomatous subjects is apparent, the average diameter of the papule in the former being 8.7 mm and that in the latter, 2.7 mm. The emulsion of normal mouse brain produced no reaction which could be regarded as positive in any group of subjects, and the reactions obtained therewith approximated the responses to antigen prepared from lymphogranulomatous mouse brain in subjects who had never had the disease.

The papules produced by individual positive reactions ranged from 7 mm to 30 by 22 mm in diameter, 77 per cent of them being from 7 to 10 mm in diameter. The latter figure agrees with that observed by Frei as the average size of the papule in persons with lymphogranuloma inguinale. The upper limit of the size of the papule in negative reactions obtained with material prepared from either normal or infected mouse brain was 5 mm and was seen in six persons only.

Patients with Inflammatory Inguinal Adenitis and Rectal Disease. That the Frei test as performed with antigen prepared from lymphogranulomatous mouse

brain is specific for lymphogranuloma inguinale is brought out by the data given in parts 2, 4 and 6 of table 1. Subjects with inflammatory inguinal adenitis and rectal disease in whom etiologic agents or conditions other than lymphogranuloma inguinale were demonstrated responded no differently to antigen prepared from lymphogranulomatous mouse brain than did nonlymphogranulomatous persons without inguinal adenitis or rectal disease. Their reactions could in no way be confused with the positive reactions of persons with the active inguinal or rectal type of the disease.

No significant difference was observed between the average size of the papule in positive reactions of patients with active lymphogranuloma inguinale of the inguinal type and that of patients who had recovered from the disease (parts 2 and 3, table 1). The central papule was, on the average, slightly smaller in patients with the anorectal type than in those with the inguinal type, but this difference was no greater than that seen among the various groups of patients with negative responses.

Patients with Syphilis. The presence of active or arrested syphilis had no influence on the reaction to antigens prepared from lymphogranulomatous mouse brains in persons who were or were not at the same time sensitized to the virus of lymphogranuloma inguinale. Lymphogranulomatous persons with syphilis showed on an average a papule 8.9 mm in diameter, while nonlymphogranulomatous persons with syphilis manifested a 2.5 mm papule. These figures are presented in parts 5 and 6 of table 1.

Results of Other Observations.—Other observations that we have made in this study have included (1) the quality of positive reactions to antigens prepared from mouse brain as compared with those to antigens prepared from pus from human subjects, (2) the possibility of desensitization to the virus or of sensitization to the virus or to the protein of mouse brain after repeated inoculations of antigen prepared from mouse brain in the same person, and (3) the keeping quality of antigen prepared from mouse brain. These observations will be dealt with in order.

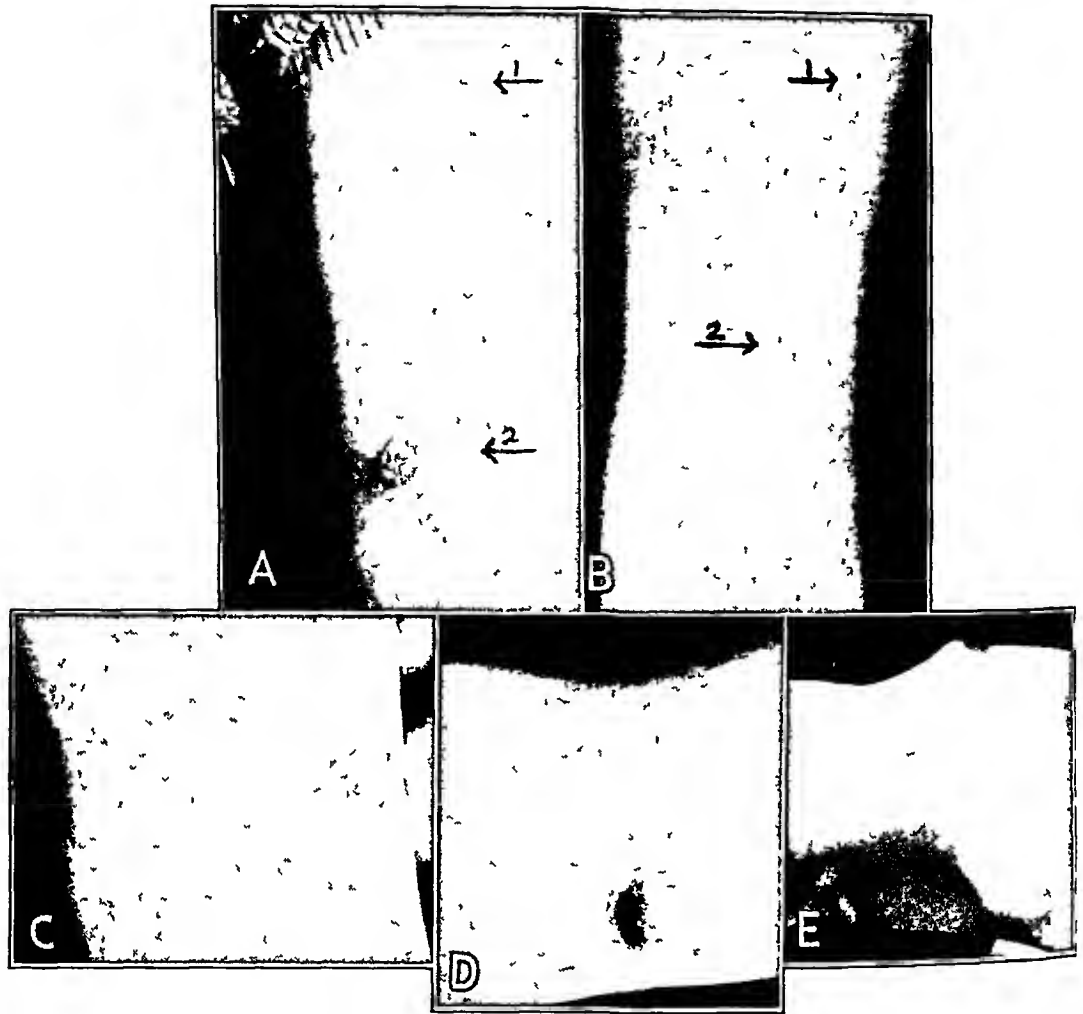
Comparison of Reactions to Antigen Prepared from Mouse Brain and Antigen Prepared from Pus from a Human Subject. The positive reaction to antigen prepared from mouse brain was in most instances qualitatively more intense than the reaction produced by antigen prepared from pus from a human subject. The central papule was higher and more scarlet and was more likely to have a relatively large vesicular or pustular center, which sometimes became necrotic; also, the area of erythema immediately surrounding the papule was usually brighter and more extensive. The reactions generally began to recede by the fourth day, ultimately leaving a slightly pigmented area or a small scar. Infrequently, diffusely papillated erythematous areas about 1 cm in diameter were encountered instead of a single central papule.

The cause of pustulation in Frei reactions has not been definitely determined. Strauss and Howard²¹ on slender evidence expressed the belief that it is due to the incomplete absorption of antigenic material. Our unpublished observations have indicated that it is a manifestation of a strong reaction.

Desensitization of Human Skin Following Repeated Intradermal Inoculations of Antigen Prepared from Mouse Brain. Wien and Perlstein²² reported tem-

21 Strauss M. and Howard M. E. The Frei Test for Lymphogranuloma Inguinale, *J. A. M. A.* **103**:1830 (Dec. 15) 1934.

22 Wien M. S. and Perlstein M. O. Intradermal Treatment of Lymphogranuloma Inguinale *Arch. Dermat. & Syph.* **28**:42 (July) 1933.



A, seventy-two hour reaction to antigens prepared from normal mouse brains and from lymphogranulomatous mouse brains in a patient with active lymphogranuloma inguinale of the inguinal type 1 indicates the low papule, 4 by 4 mm, produced by inoculation with an emulsion of normal mouse brains 2 indicates the infiltrated erythematous area, 20 by 20 mm, surmounted by a vesicle 10 by 9 mm, produced by inoculation with antigen prepared from lymphogranulomatous mouse brains *B*, forty-eight hour reaction to an emulsion of normal mouse brains and to antigen from lymphogranulomatous mouse brains in a nonlymphogranulomatous subject 1 indicates the low papule, 3 by 4 mm, produced by inoculation with the emulsion of normal mouse brains 2 indicates the low papule, 4 by 5 mm, produced by inoculation with antigen prepared from lymphogranulomatous mouse brains *C*, seventy-two hour reaction to antigen prepared from lymphogranulomatous mouse brains in a patient with anorectal lymphogranuloma inguinale There was an erythematous papule 10 mm in diameter The reaction to an emulsion of normal mouse brains in this subject was a 3 by 2 mm nonerythematous low papule *D*, seventy-two hour reaction to antigen prepared from lymphogranulomatous mouse brains in a very strong reactor There was an erythematous papule 30 by 22 mm, rising 7 mm from the surface of the skin, the center contained a 7 mm vesicle The reaction to an emulsion of normal mouse brains in this patient, who presented the anorectal type of the disease was a nonerythematous low papule 2 by 3 mm *E*, lateral view of the papule depicted in figure *D*, showing the unusual height of the papule

porary local desensitization of the skin of a patient to the virus of lymphogranuloma inguinale after repeated intradermal inoculations of Frei antigen prepared from pus from a human being. In our series of cases, ten lymphogranulomatous subjects received five or more intradermal inoculations of antigen prepared from mouse brain at various intervals, and in none did the repetition of the test produce any diminution in the size and quality of the reaction. Practically all these tests were performed on both the upper and the lower part of the arm, four segments of the limb were thus available, and successive tests were seldom performed on the same segment. It is probable that failure to produce local desensitization was due to the long interval which elapsed between successive inoculations of the same segment. The data relating to this series of inoculations are set forth in table 2.

Sensitization of Human Skin to the Protein of Mouse Brain A review of the reactions to antigen prepared from normal mouse brain in all our subjects showed that none possessed a natural hypersensitivity to the protein of mouse brain. There was, however, the possibility of effecting an acquired hypersensitivity

TABLE 2—*Intervals Between Successive Inoculations of the Same Segment of the Arm*

Subject	Type of Lymphogranuloma Infection	Number Performed	Frei Tests	
			Shortest Interval Between Successive Tests on Same Segment, Days	Interval Between First and Last Tests, Months
MeG	Anorectal	18	32	10
B	Anorectal	16	65	8
G	Inguinal	9	16	7
J	Anorectal	9	17	10
R	Anorectal	9	90	3
A	Inguinal	8	5	1
L	Inguinal	8	72	5
C	Inguinal	7	76	5
O	Inguinal	6	No repetition on same segment	4
E	Inguinal	5		2

by the repeated inoculation with antigen over a period of months. Hence the reactions of all subjects, particularly of those listed in table 2, were studied with this point in mind. One person only (G), after receiving nine tests in a period of seven months, exhibited a somewhat larger papule and a more intense positive response at the end of that time. That this increase was due to an acquired hypersensitivity to the protein of mouse brain was evident from the fact that his concurrent reaction to material prepared from normal mouse brain was a 5 mm papule with a surrounding flare 40 mm in diameter. His earlier reactions to normal mouse brain showed only average-sized papules. None of the sixty-four other subjects exhibited a similar phenomenon. It is felt, therefore, that whereas an acquired hypersensitivity to the protein of mouse brain might be produced by the repeated use of the antigen in the same person for diagnosis, it probably occurs infrequently and then is of insufficient degree to produce a false positive result. Not enough inoculations of nonlymphogranulomatous subjects with antigen prepared from lymphogranulomatous mouse brains have been performed to make valid any statement as to the possibility of producing sensitization to the virus.

The Keeping Quality of Antigen Prepared from Mouse Brain All the antigens were tested in human subjects within one month after preparation, and several were tested as long as eight months later. None had shown any decrease in potency or standing for that length of time.

COMMENT

Antigen prepared from mouse brain infected with the virus of lymphogranuloma inguinale can replace that prepared from pus from a human being for the performance of the Frei test. This statement is based on the results of 95 tests on twenty-seven lymphogranulomatous persons and of 105 tests on thirty-eight nonlymphogranulomatous persons. Eighty-eight different specimens of antigen were used, which were prepared from the brains of mice used for the second to the forty-fourth passage of a single strain of the virus. The tests were carried out over a period of one year. By proper dilution of antigen prepared from mouse brain it was possible to obtain results which agreed closely with those obtained by the use of antigen prepared from pus from a human being. The average diameter of the papule in a positive reaction was 8.7 mm, and that in a negative reaction, 2.7 mm. The sensitivity of the antigen prepared from mouse brain was as high as that of the most potent antigens prepared from pus from our patients. No instance was found in which the cutaneous effect of the protein of the mouse brain could be regarded as producing a false positive reaction. Earlier in this paper it was pointed out that one of the chief disadvantages of antigen prepared from pus from a human subject is the possibility of the presence in the pus of other organisms which are difficult to demonstrate. Antigen prepared from mouse brain has not this disadvantage. Mice, however, suffer from spontaneous encephalitis of virus origin²³ and can harbor the virus of choriomeningitis without showing any sign of its presence. The latter virus has been studied by Traub²⁴ and Armstrong²⁵ and has been shown by Rivers²⁶ to be identical with the causative agent of a form of meningitis in man. Infectious ectromelia of mice²⁷ need not be considered here.

During the course of this work we have been aware of the possibility of the coexistence of a virus disease like that of Theiler,²³ Armstrong,²⁵ and Traub,²⁴ along with our strain of the virus of lymphogranuloma inguinale. Such a virus could have been latent in our stock mice and picked up some time during intracerebral passage of the virus of lymphogranuloma inguinale or could have been obtained from the original

23 Theiler, Max. Spontaneous Encephalitis of Mice. A New Virus Disease, *Science* **80** 122 (Aug. 3) 1934.

24 Traub, E. A Filterable Virus Recovered from White Mice, *Science* **81** 298 (March 22) 1935.

25 Armstrong, C., and Lillie, R. D. Experimental Lymphocytic Choriomeningitis of Monkeys and Mice Produced by a Virus Encountered in Studies of the 1933 St. Louis Encephalitis Epidemic, *Pub. Health Rep.* **49** 1019 (Aug. 31) 1934.

26 Rivers, T. M., and Scott, T. F. McNair. Meningitis in Man Caused by a Filterable Virus, *Science* **81** 439 (May 3) 1935.

27 Marchal, J. Infectious Ectromelia, *J. Path. & Bact.* **23** 713, 1930.

human inoculums We have examined our material carefully with this point in mind and shall describe our observations under the two following headings

Experiments with Normal Stock Mice (Rockland Farms)—Following the technic of Traub,²⁴ 200 stock mice were inoculated with 0.03 cc of sterile broth intracerebrally in an attempt to activate a latent infection Only negative results were obtained Also, in connection with our experiments on the transmission of the virus of lymphogranuloma inguinale, in no instance were there observed any signs of illness in the control animals which received intracerebral inoculations of a physiologic solution of sodium chloride, Tyrode's solution, ascitic fluid, broth of pH 8, heated emulsion of infected mouse brain or emulsion of normal mouse brain

Observations on Mice Inoculated with the Virus of Lymphogranuloma Inguinale—The signs observed in these animals were the same in each generation and much like the signs reported by other investigators There was nothing to indicate the presence of any unusual element in the condition Traub²⁸ has also recently carried out cross-immunity and cross-neutralization experiments with our strain of the virus of lymphogranuloma inguinale and the virus of choriomeningitis and has shown the two viruses to be immunologically distinct

We feel, therefore, that the antigens prepared from mouse brains used in this work contained no other virus than that of lymphogranuloma inguinale We are of the opinion, also, that the likelihood of introducing an extraneous virus is negligible provided that mice of the same clean stock obtained from a single reliable breeder are always used and that these mice are tested periodically for the presence of latent virus disease

SUMMARY

It has been found that Frei antigen can be prepared from the brain of a mouse infected with the virus of lymphogranuloma inguinale

The original Frei antigen as prepared from pus from a human being has many drawbacks

There are at least four distinct conditions due to lymphogranuloma inguinale which may be diagnosed by the performance of the Frei test

Antigen prepared from mouse brain has been tried for one year at the New York Hospital for the diagnosis of lymphogranuloma inguinale The preparation and administration of eighty-eight different specimens of antigen, derived from the brains of mice used for the second to the forty-fourth passage of a single strain of virus, and the results of their use in twenty-seven patients with the disease and in thirty-eight nonlymphogranulomatous subjects are described in detail

The average positive reaction to antigen prepared from mouse brain was an erythematous papule 8.7 mm in diameter, with a surrounding flare of varying size, 77 per cent of these reactions showed a central papule from 7 to 10 mm in diameter

28 Traub, E Personal communication to the authors

No reaction which could be regarded as positive was obtained in any person by the use of antigen prepared from lymphogranulomatous mouse brain in nonlymphogranulomatous persons or by the use of emulsions of normal mouse brain, prepared in the same way as the antigen

The results of tests on patients with conditions which must be differentiated from lymphogranuloma inguinale were definitely negative

The presence of active or arrested syphilis had no effect on the reaction to the Frei test performed with antigen prepared from mouse brain

By standardization of dilution and dosage it was possible to produce reactions quantitatively the same as those to antigens prepared from human pus, qualitatively, however, the reactions were usually more intense

No desensitization of the skin of any lymphogranulomatous subject was observed after repeated inoculations with antigen prepared from mouse brain. Low grade sensitization to the protein of mouse brain, however, was seen in one instance

Antigen prepared from mouse brain has been found to retain its potency for at least eight months after preparation

Experiments have been performed to detect the coexistence of spontaneous virus disease of mice with our strain of the virus of lymphogranuloma inguinale. Only negative results have been obtained

It is felt, therefore, that antigen prepared from lymphogranulomatous mouse brain can replace that prepared from pus from a human being for the diagnosis of lymphogranuloma inguinale. Not only is it as sensitive and specific as the most potent antigen prepared from human material, but it overcomes the disadvantages of the latter

STUDIES IN THE GENUS MICROSPORUM

II BIOMETRIC STUDIES

NORMAN F CONANT, PH D

DURHAM, N C

Attempts to present the morphologic characters of the dermatophytes for the purpose of making their identification easier have not resulted in a classification which clearly distinguishes the specific characters. In this respect, Ota and Langeron¹ defined genera but merely listed the species which they considered should be included in these genera. Likewise, Grigorakis,² although he treated specific characters more thoroughly than the previous authors, failed to present a diagnostic key to the species studied, as he became involved in the theoretical rôle of pleomorphism among these forms.

Other attempts to classify the dermatophytes mycologically have resulted in a discussion of their possible relationship to the Gymnoascaceae. In this respect, Matruchot and Dassonville,³ Nannizzi⁴ and Langeron and Milochevitch⁵ have in turn compared the morphologic similarities of the two groups and have proposed a classification in which the dermatophytes have been included among the Gymnoascaceae. To make such a classification effective, the ascospore stage in the life cycle of the dermatophytes should be found, and the similarity of this stage to that of the Gymnoascaceae should be proved. Nannizzi⁶ attempted

Contribution 140 from the Laboratory of Cryptogamic Botany and the Farlow Herbarium, Harvard University

1 Ota, M., and Langeron, M. Nouvelle classification des dermatophytes, *Ann. de parasitol.* **1** 305, 1923

2 Grigorakis, L. Recherches cytologiques et taxonomiques sur les dermatophytes, *Ann. d. sc. nat. bot.* **7** 165, 1925

3 Matruchot, L., and Dassonville, C. Sur le champignon de l'herpes et les formes voisines et sur la classification des ascomycetes, *Bull. Soc. mycol. de France* **15** 240, 1899, Sur le *Ctenomyces serratus* Eidam compare aux champignons des teignes *ibid.* **15** 305, 1899, Sur une forme de reproduction d'ordre eleve chez le trichophyton, *ibid.* **16** 201, 1900

4 Nannizzi, A. Ricerche sui rapporti morfologici tra Gymnoascaceae e Dermatomiceti *Ann. mycol.* **24** 85, 1926

5 Langeron, M., and Milochevitch, S. Morphologie des dermatophytes sur milieu naturels et milieu a base de polysaccharides. Essai de classification *Ann. de parasitol.* **8** 465, 1930

6 Nannizzi, A. Ricerche sull' origine saprofitica dei funghi delle tigne II *Gymnoascus gypseus* sp. n. forma ascofora del Sabouraudites (*Achorion*) *gypseus* (Bodin) Ota and Langeron, *Atti d. r. Accad. d. fisiocrit. in Siena* **2** 89, 1927

to do this when he reported the finding of ascospores in *Achorion gypseum* Tate,⁷ however, could not confirm this report, nor have others been able to do so. It therefore appears to me that, since ascospores are not produced and the fungi therefore cannot be described with regard to these stages, it is more desirable to base the classification of the dermatophytes on structures which are found, namely, the imperfect asexual spore forms.

Among the fungi imperfecti certain groups have been studied and classified on the basis of the type and character of the spores produced, the manner in which they are borne and the arrangement and character of their supporting structures. Such studies have resulted in a usable classification of this group of fungi. I have therefore studied species of the genus *Microsporum* for the purpose of presenting diagnostic characters which will enable identification of cultures.

MORPHOLOGY OF THE GENUS MICROSPORUM

That the dermatophytes differ in their type of growth and ability to produce spore forms on various artificial mediums has been pointed out several times. Because of this, Grigorakis² studied only "mother cultures," or primary isolations. When this method is used he expressed the belief that the characters first presented on culture are the true characters of the fungi, whereas in subsequent transfers the spore forms and other features are lost. This loss of distinguishing spore forms has greatly hindered prolonged morphologic studies of the fungi of the skin in many instances. It has been found, however, that in many cases the fungi do not produce characteristic spore types when first cultured. Davidson, Dowding and Buller⁸ have shown that spores have been produced in some of their cultures only after several transfers. I have also found that a great many cultures do not at first produce the spore types of the genus *Microsporum*.

It was necessary, therefore, to secure a consistent growth of species of *Microsporum* in culture before a detailed study of the spore forms and attendant mycelial characters could be used for specific differentiation. With this in mind I⁹ studied several cultures and found that a consistent production of spore forms in the genus *Microsporum* could be induced in rice cultures. On this medium the heavily sporulating mats of mycelium readily yielded material for study.

7 Tate, P. The Dermatophytes or the Ringworm Fungi, *Biol. Rev.* 4:41, 1929.

8 Davidson, A. M., Dowding, E. S., and Buller, A. H. R. Hyphal Fusions in Dermatophytes, *Canad. J. Research* 6:1, 1932.

9 Conant, N. F. Studies in the Genus *Microsporum*. I. Cultural Studies, *Arch. Dermat. & Syph.* 33:665 (April) 1936.

In rice cultures the most characteristic spore form produced was the long, tapering, spindle-shaped multicellular spore called a fuseau (fig 1, 1) This large spore, or macroconidium, appeared terminally on the aerial hyphae, whereas the small single-cell spores, the aleuries or microconidia (fig 1, 3), were borne laterally along the hyphae Also in the aerial hyphae and in cultures grown on the "natural mediums" of Langeron and Milochevitch,⁵ were long slender spirals (fig 1, 2) These spirals are characteristic of a great many fungi of the genus *Trichophyton* In the mycelial mat were seen chlamydospores (fig 1, 7), the large thick-walled resting spores, raquet hyphae (fig 1, 6) with enlarged, swollen distal ends and pectinate hyphae (fig 1, 5), which were short comblike formations with projections on the curved periphery In addition to these bodies which occurred regularly, a structure seen in many of the *Microspora* was the so-called nodular

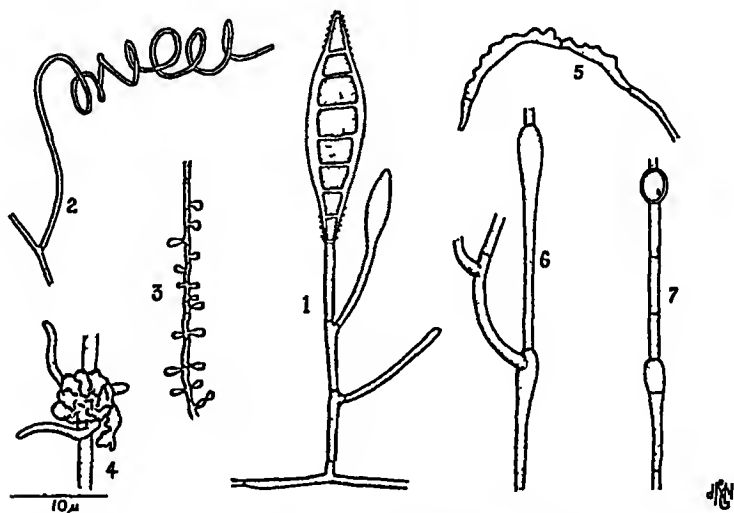


Fig 1—Representative structures in the genus *Microsporum* 1, mature macroconidium (fuseau) seen in optical section (the immature macroconidium begins as a swelling at the apex of the side branch), 2, spiral hypha, 3, laterally borne microconidia, 4, nodular body, 5, pectinate hypha, 6, raquet hypha, 7, chlamydospore, a thick-walled resting spore

body (fig 1, 4) This structure was the result of the intertwining and knotting of mycelial branches either from the same hyphal strand or from those adjacent At times this body was represented only by a coiling of one hyphal strand around another, and hence by some investigators this structure has been thought to bear some resemblance to the ascogonial coil found in the *Ascomycetes* However, it has never been seen to mature into an ascus-producing body

COMPARISON OF MACROCONIDIA IN THE GENUS MICROSPORUM

Since the macroconidium (fuseau) is the most important spore form of the genus *Microsporum*, its value as a diagnostic specific character

must be established if a usable taxonomic treatment of the genus is to be based on it. Distinctive characters of the spores, such as the size, shape, color and thickness of the wall, the nature of the surface of the wall (whether smooth or echinulate), the septations and the manner in which the spores are borne from their supporting structures must be taken into consideration in an effort to find specific differences. While searching for these characters in a number of cultures, I was impressed with the great variation in length and width and in the number of septations seen in macroconidia from the same culture. Such a condition, however, is present not only in the genus *Microsporum* but in other members of the group of fungi imperfecti.

In view of a plasticity of diagnostic structures in other groups of fungi, they have been studied to determine the degree of variation and the means by which the variation may best be expressed. For this purpose, biometric studies of the types of reproductive bodies observed in culture or elsewhere have been resorted to in order to group or to distinguish forms which appear too closely related for satisfactory separation otherwise. In this way, Rosenbaum¹⁰ and Tucker¹¹ studied the genus *Phytophthora* and Braun¹² the genus *Pythium*. In the rusts Stakman and Piemeisel,¹³ Stakman and Levine¹⁴ and Levine¹⁵ found that physiologic forms could be identified on the basis of their morphology if measurements were taken from material grown under favorable conditions and on congenial hosts. In the fungi imperfecti, to which the dermatophytes belong, the same type of study has been applied to *Helminthosporium*. In this genus the large septate spores are not unlike those of *Microsporum*. By means of a biometric study (length, width and number of septations) of the conidia of two species

10 Rosenbaum, J. Studies of the Genus *Phytophthora*, J Agric Research 8 233, 1917

11 Tucker, C. M. Taxonomy of the Genus *Phytophthora* de Bary, Research Bulletin 153, Agric Exper Stat, University of Missouri, 1931

12 Braun, H. Comparative Studies of *Pythium debaryanum* and Two Related Species from *Geranium*, J Agric Research 30 1043, 1925

13 Stakman, E. C., and Piemeisel, F. J. Biologic Forms of *Puccinia graminis* on Cereals and Grasses, J Agric Research 10 429, 1917

14 Stakman, E. C., and Levine, M. N. Effect of Certain Ecological Factors on the Morphology of Urediospores of *Puccinia graminis*, J Agric Research 16 43, 1919

15 Levine, M. N. A Statistical Study of the Comparative Morphology of Biologic Forms of *Puccinia graminis*, J Agric Research 24 539, 1923. Biometrical Studies of the Variation of Physiologic Forms of *Puccinia tritici* and the Effects of Ecological Factors on the Susceptibility of Wheat Varieties, Phytopath 18 7, 1928

of *Helminthosporium*, Nisikado and Miykade¹⁶ found reliable diagnostic differences which had not at first been apparent

Since such a successful application of biometrics has been made in various other groups of fungi, I have attempted to apply this type of study to *Microsporium*

The fungi were grown on polished rice in flasks made up with one part rice to three parts water and sterilized in free steam for one hour on two successive days. Bits of the sporulating mycelium from these flasks were carefully teased apart in lactophenol cotton blue. In these mounts the macroconidia were carefully measured, and curves were plotted for the various species. By the use of these simple curves it was found that the characteristic size of the spores of a given species could be more easily recognized, while at the same time a comparison of the curves would lead to a differentiation of the species.

The cultures studied and the sources from which they were received have been listed elsewhere,⁹ and the same groupings will be used in this paper.

- Group I *Microsporium fulvum* 483,24, *Microsporium gypseum* 12,12a,13
- Group II *Microsporium lanosum* 19,27,29,33,486
Microsporium felneum, 5, 481
- Group III *Microsporium equinum* 50, 485
- Group IV *Microsporium obesum* 40
Microsporium aurantiacum 43
Microsporium simiae 80
Microsporium pseudolanosum 42

The macroconidia of these cultures seemed to be grouped together into eight categories, based not alone on their size but also on their shape, the thickness of their walls and the amount of roughness. The microscopic aspect of these macroconidia may be seen in figure 2. The spores in this figure demonstrate the degree of variability in the single species as well as the degree of similarity between different species. It will be seen that *A* and *D*, *B* and *E*, and *C* and *F* differ markedly not only in size but in shape and in the amount of roughness. The first six groups may be seen to differ from groups *G* and *H* in size and in the thickness of their walls. However, *A*, *B* and *C* are similar in all respects, as are *D*, *E* and *F*, and *G* and *H*. When such similarities exist, real differences are demonstrated only when great numbers of specimens are considered and a quantitative means of comparison is employed.

Such a means of comparison is that of curves in which the sizes of the spores are plotted against the number of the spores measured. The fungi of group I, *M. fulvum* and *M. gypseum*, have the small thin-walled type of macroconidium (fig. 2 *G* and *H*). Macroconidia from six different isolations of these two species were studied and measured to determine if two clearcut species existed. For this purpose 200 macroconidia each of *M. gypseum* 12, 12a and 13 were compared with a like number of macroconidia of *M. fulvum* 24, 483 and an additional strain not on the list, *M. fulvum* N. Y. The curves of the length of the macroconidia of these six isolates are plotted in figure 3. The size interval includes 2 microns. I.e., spores were grouped together which fell within the length of from 28 to 30

16 Nisikado, Y. and Miykade, C. Studies on Two *Helminthosporium* Diseases of Maize Caused by *H. turcicum* Passerini and *Ophiobolus heterostrophus* Drechsler (= *Helm. Maydis* Nisikado et Miykade), Ber. Ohara Inst. 3: 221, 1926.

microns, from 30 to 32 microns, and so forth. It will be seen in figure 3 that the three isolations of *M. fulvum* 24, 483 and N Y fall into one group, with peaks at from 38 to 40 microns, while *M. gypseum* 12, 12a and 13 fall into another group with peaks at from 44 to 46 microns. To bring out these differences more clearly, a regrouping of the count in figure 3 was made so that 600 macroconidia of one group were compared with 600 macroconidia of the other. The curves for this grouping presented in figure 4 indicate two distinct species, *M. fulvum* having a definite peak at 38 microns and *M. gypseum* having a definite peak at 44 microns. Such a difference in the two species had not been readily apparent heretofore, as these two species have been considered morphologically identical (Ota and Langeron¹ and Grigorakis¹⁷). These authors, however, did not reduce either to synonymy but maintained both specific names.

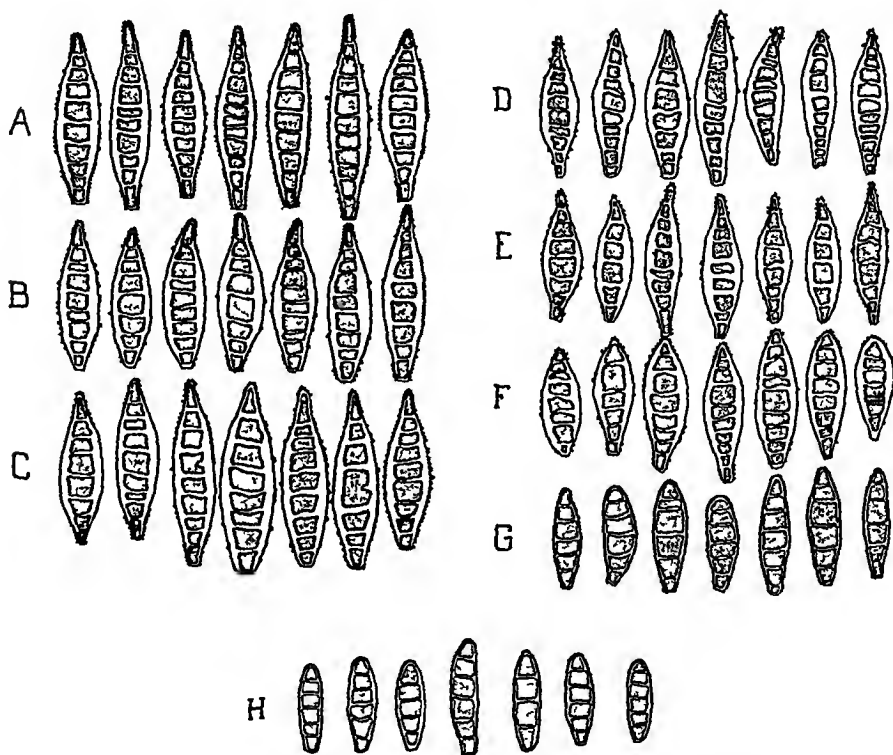


FIG 2—Representative macroconidia in eight species of *Microsporium*, demonstrating the variations in length, width, number of septations and roughness of the walls. A, *Microsporium lanosum*, B, *Microsporium pseudolanosum*, C, *Microsporium aurantiacum*, D, *Microsporium equinum*, E, *Microsporium simiae*, F, *Microsporium obesum*, G, *Microsporium gypseum*, H, *Microsporium fulvum*.

In the same manner the curves of the spores of *M. lanosum* and *M. felineum* of group II were compared. In this comparison the curves of the lengths of 200 macroconidia each from four isolations of *M. lanosum* 486, 19, 27 and 33 and 200 macroconidia from *M. felineum* 5 are presented in figure 5. It will be seen that the curves of *M. lanosum* 486, 19 and 27 and *M. felineum* 5 show a close agreement. The curve for *M. lanosum* 33, however, attains a peak of 78 microns,

¹⁷ Grigorakis. *Dermatophytes et dermatomycoses*, *Ann de dermat et syph* 10 18, 1929, footnote 2.

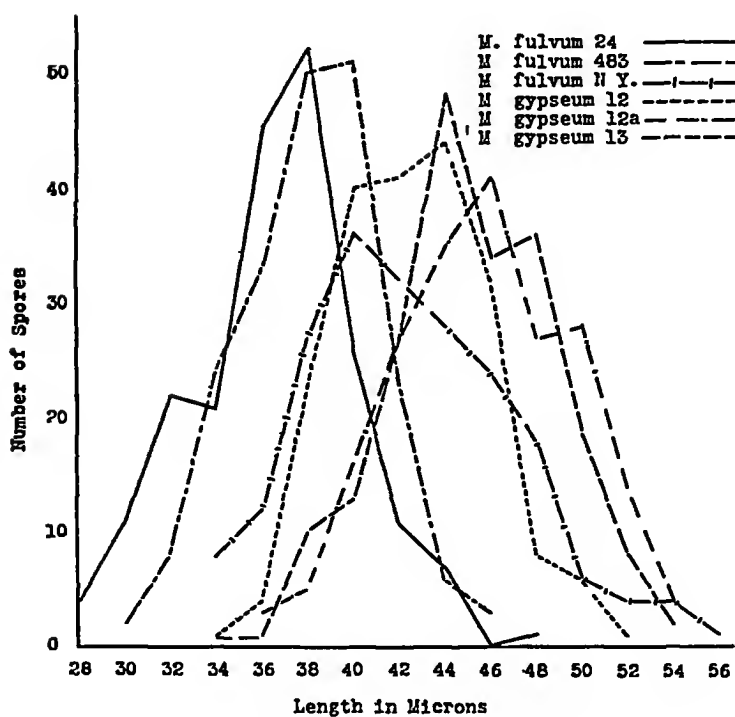


Fig 3—Comparison of the lengths of 200 macroconidia each of three isolations of *M. fulvum* and three of *M. gypseum*

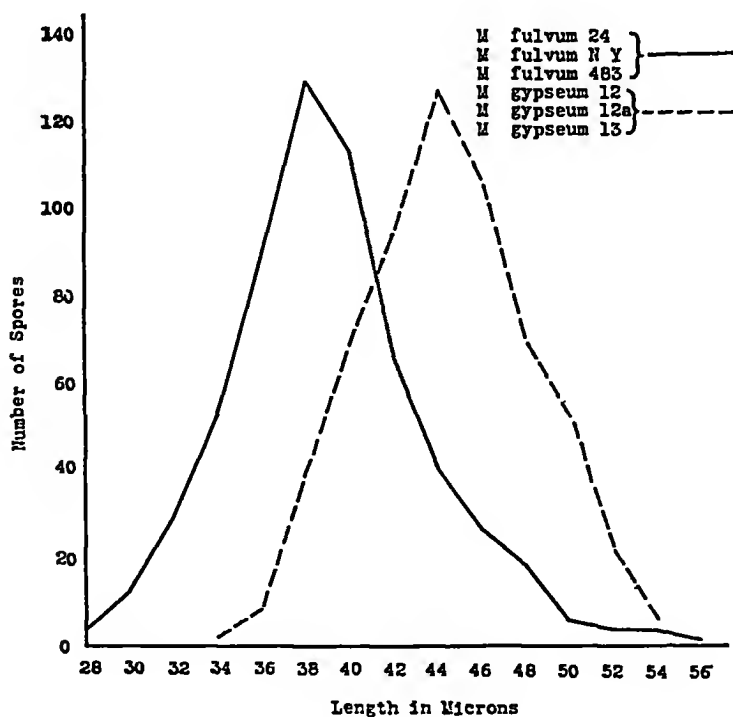


Fig 4—Comparison of the lengths of 600 macroconidia 200 each from *M. fulvum* 24, N Y and 483, 200 each from *M. gypseum* 12, 12a and 13

although its range lies within that of the other curves. Because of the similarity of the curves in these isolations, I considered *M lanosum* and *M felineum* as one species. The marked similarity of these two fungi has been noted before. While most authors have kept the two specific names *lanosum* and *felineum*, Langeron and Milochévitch⁵ reduced the two to synonymy and retained as the valid name *M felineum*, as they considered it the first named species.

A comparison of the curves of groups III and IV is presented in figure 6. The spores of these species (*M obesum*, *M simiae*, *M equinum*, *M pseudolanosum* and *M aurantiacum*) took an intermediate position between the limits of

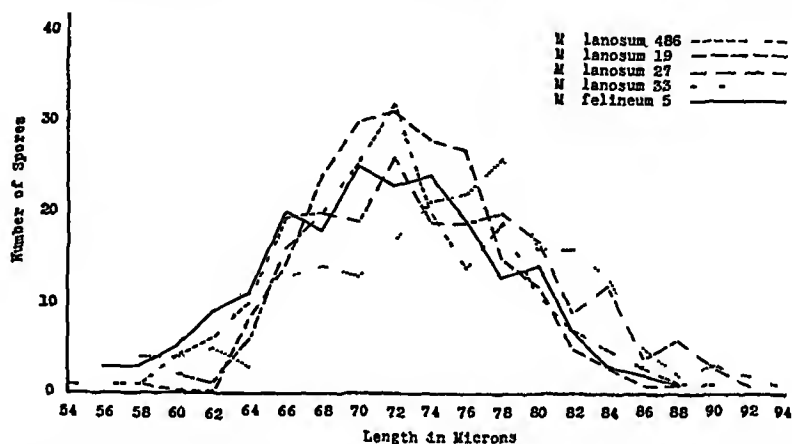


Fig 5 Comparison of the lengths of 200 macroconidia each from four isolations of *M lanosum* and one isolation of *M felineum*

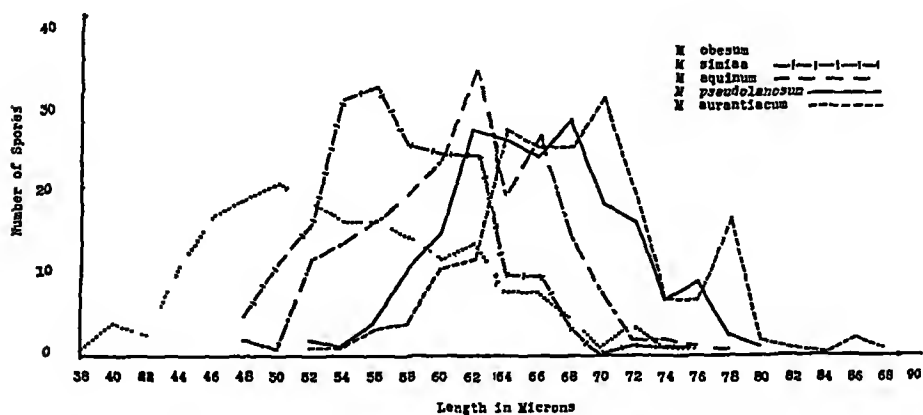


Fig 6—Comparison of 200 macroconidia each of *M obesum*, *M simiae*, *M equinum*, *M pseudolanosum* and *M aurantiacum*

28 and 94 microns of the spores of *M fulvum* and *M lanosum*, respectively. In figure 6 it is seen that the majority of the spores of *M obesum* fall within the limits of from 48 to 56 microns, *M simiae*, from 54 to 58 microns, *M equinum*, from 62 to 66 microns, *M pseudolanosum*, from 64 to 68 microns, and *M aurantiacum*, from 64 to 72 microns. In this figure at least four curves (those for *M obesum*, *M simiae*, *M equinum* and *M aurantiacum*) are sharply defined and distinct, showing that the size of the macroconidia may be used for purposes of specific differentiation. The curve for *M pseudolanosum*, however, is in close agreement with those for *M equinum* and *M aurantiacum*. However, although

the macroconidia may be similar in size, other characters immediately separate these three species. *M. pseudolanosum* was easily distinguished from *M. aurantiacum* because of the rusty to orange spores of *M. aurantiacum*, while in *M. pseudolanosum* the spores were light buff. *M. equinum* also was distinguished easily from *M. pseudolanosum*. In *M. equinum* the macroconidia were borne from their supporting structures (conidiophores) in clusters, while in the latter a looser type of spore bearing was evident. A more detailed description of the several species mentioned in this paper, a description including not only the sizes of the spores but other distinguishing morphologic characters, will appear in a later paper.

For a better understanding of the relation of the curves considered in these various figures, a graph of all the curves is presented in figure 7. Here it will be seen that certain groupings are clearcut. For example, two species are indicated at the extreme left of the graph: one species to include *M. fulvum*, with spores of an average size of from 38 to 40 microns, the other to include *M. gypseum*, with spores of an average size of from 44 to 48 microns. Other curves in figure 7 show a third species, *M. obesum*, with spores from 48 to 56 microns long, a fourth species, *M. simiae*, with spores from 54 to 58 microns long, a fifth species, *M. equinum*, with spores from 62 to 66 microns long, and a sixth species, *M. lanosum*, with spores from 70 to 76 microns long. These curves are distinct, while the somewhat overlapping curves for *M. pseudolanosum* and *M. aurantiacum*, with spores averaging from 64 to 68 microns and from 64 to 72 microns in length, respectively, are not so convincing as to species rank. However, the additional characters which have been mentioned, i. e., the color of the macroconidia and the methods by which they are borne, are fully adequate for purposes of specific differentiation.

SUMMARY

Studies to make possible the identification of species in the genus *Microsporum* involved a cultural, biometric and taxonomic consideration of a number of cultures. First, it was necessary to secure a consistent growth of the species on an artificial medium. Such a medium proved to be polished rice, on which a luxuriant growth was maintained which produced morphologic characters serving to distinguish the species. One such distinguishing character produced on rice was the large pluriseptate, fusiform, thick-walled spore, the macroconidium or fuseau. This spore was produced constantly and in great numbers. A more detailed discussion of the cultural study of this group of fungi has been given in a previous paper.⁹

Since the macroconidia proved to be the most prominent character of the genus, it was studied with the hope that it might be used in distinguishing species. Thus, the second consideration in this study of the genus *Microsporum* involved a biometric study of the Macroconidia, because of their variability in size. For this purpose the sizes of the spores were plotted for the various cultures studied. By comparing these curves six species were apparent: *M. fulvum*, *M. gypseum*, *M. obesum*, *M. simiae*, *M. equinum* and *M. lanosum*. The curves for *M. pseudolanosum* and *M. aurantiacum* were not as convincing as to

species rank. Fortunately, however, additional morphologic characters are available which, when taken as a whole, tend to strengthen the concept of a given species. Such characters as color of the spore, general shape, thickness of the wall, type of the wall (whether smooth or echinulate), the manner in which the spores are borne on their supporting structures (conidiophores) and the type of conidiophore all are necessary for a complete and easy segregation of species in any group of the fungi imperfecti.

Thus a third consideration in the study of the genus *Microsporum* would involve the gathering of all morphologic data and their presentation in a truly taxonomic treatment of the genus. With the foundation of a cultural and biometric study of several cultures, I have prepared such a taxonomic treatment for *Microsporum*, in which all the available morphologic characters will be considered and a key to the species will be presented, with the hope that it may prove of value to other investigators. This final paper will appear later.

This work was carried on under the direction of Prof. W. H. Weston, Jr.

LXXIV SENSITIZATION OF ANIMALS TO PLANT OILS

ROY L KILE, M D

ST LOUIS

Bloch and Steiner-Wourlisch¹ were the first to sensitize guinea-pigs to primrose by contact. Since then Mayer² has sensitized them in the same manner to para-phenylene-di-amine, Jadassohn,³ to phenylhydrazine, and Simon and his associates,⁴ to poison ivy oil. That sensitization can be produced in certain human beings by repeated contact with a substance has been shown by Strauss,⁵ who sensitized infants to poison ivy, by Muller,⁶ who used ursol (para-phenylene-di-amine), and by Silverberg,⁷ who used mesotan (the methyloxymethyl ester of salicylic acid). Although the mechanism for producing hypersensitivity in man may not be the same, the condition occurs in a manner parallel to that noted in animals.

After a study of guinea-pigs sensitive to ivy, Simon and his associates⁴ pointed out that the entire skin of the animal seemed to be sensitized. This was also noted by Bloch and Steiner-Wourlisch¹ with guinea-pigs sensitive to primrose and it is usually true in human beings. It is known, however, that there is some localization of contact sensitization in human beings, as can be shown at times with patch tests on various areas over the body. It is also not unusual to find contact dermatitis exclusively on one part of the body, such as the face, although

Studies, observations and reports from the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, Department of Dermatology, service of Drs M F Engman and W H Mook

The oils used in this work were prepared in collaboration with Morris Moore, Ph D, mycologist to the Barnard Free Skin and Cancer Hospital

1 Bloch, B, and Steiner-Wourlisch, A. Die Sensibilisierung des Meerschweinchens gegen Primeln, *Arch f Dermat u Syph* **162** 349, 1930

2 Mayer, R L. Die Ursolidiosyncrasie des Meerschweinchens, *Arch f Dermat u Syph* **163** 223, 1931

3 Jadassohn, W. Sensibilisierung der Haut des Meerschweinchens auf Phenylhydrazin, *Klin Wchnschr* **9** 551, 1930

4 Simon, F A, Simon, M G, Rackemann, F M, and Dienes, L. The Sensitization of Guinea Pigs to Poison Ivy, *J Immunol* **27** 113, 1934

5 Strauss, H W. Artificial Sensitization of Infants to Poison Ivy, *J Allergy* **2** 137, 1931

6 Muller, A. Sensibilisierungsversuche mit Ursol, *Dermat Ztschr* **61** 241, 1931

7 Silverberg, M G. The Sensitization of the Skin to Mesotan, *Arch Dermat & Syph* **21** 166 (Feb) 1930

several other areas, such as the hands and arms, have been exposed at the same time. However, this is usually not true when poison ivy is the contact substance.

MATERIALS AND TECHNIC

The oils used in these experiments were acetone extracts prepared as described by Brown, Milford and Coca⁸ and by Engman, Moore and Kile⁹. All solutions were made by volume in acetone.

Four guinea-pigs were painted with a 50 per cent solution of poison ivy oil after the hair had been pulled out by hand twenty-four hours previously. A stripe of oil was made across the intact skin of the abdomen with a camel's hair brush. This was repeated daily for six days. Four rabbits were treated in the same manner. Nine other guinea-pigs were treated similarly each day for three days. Four animals were painted for six days with 50 per cent dwarf ragweed oil, and six others were painted on nine successive days. Eight were painted for six days with 50 per cent orris root oil, four for six days with 50 per cent giant ragweed oil and four for six days with 50 per cent sage oil. Four guinea-pigs painted with acetone on six successive days showed no change.

Two weeks after the last application all the animals were tested by painting a stripe across the abdomen with a 5 per cent solution of the oil, as were also the control animals. Two controls were used for each group tested.

It was found that all the pigs painted six times with ivy oil exhibited a typical area of dermatitis within twenty-four hours. This persisted for forty-eight hours and slowly faded during the following week, the skin finally desquamating. The dermatitis consisted of a stripe of erythema, with tiny vesicles, at the test site. The test site need not be the site at which the previous paintings were done. Of the animals painted three times, two showed no more reaction than the controls, and two died during the experiment. At autopsy the essential change noted was acute nephritis with edema and hemorrhage into the kidney. The other organs were apparently normal. The five remaining guinea-pigs showed exactly the same reactions as those that had been painted six times. Biopsies made of the affected areas twenty-four hours after painting showed typical dermatitis, consisting of edema of the upper portion of the cutis, vascular dilatation and intracellular and extracellular edema of the epidermis, with beginning vesicle formation. The animals showed the same reaction when tested four months later. The ivy controls showed a faint, transient erythema, which disappeared within forty-eight hours and in no way approached the dermatitis produced in the treated animals.

The four animals painted six times were tested with the saponifiable and unsaponifiable fractions of the ivy oil, as well as with the whole oil. These were prepared as has been previously described⁹ and were merely the two fractions resulting from saponification with sodium. It was found that the unsaponifiable fraction produced a dermatitis similar to that produced by the whole oil, though not quite so marked. The saponifiable fraction produced no reaction.

When the four rabbits were tested with both a 5 per cent and a 25 per cent solution of ivy oil, no reaction was noted other than the transient erythema also seen on the control animals. None of the guinea-pigs painted with orris root oil, sage oil or giant ragweed oil, or the controls, showed any reaction on

8 Brown, A., Milford, E. L., and Coca, A. F. *Studies in Contact Dermatitis*, *J. Allergy* **2** 301, 1931.

9 Engman, M. F., Jr., Moore, M., and Kile, R. L. *Contact Dermatitis*, *South M. J.* **28** 442, 1935.

being tested with 5 per cent, 12.5 per cent and 25 per cent dilutions. Eight of the ten guinea-pigs treated with dwarf ragweed oil showed no reactions to the same dilutions. However, two of the animals showed an area of dermatitis when tested with 5 per cent and 25 per cent dilutions. This persisted for several days and was definite, though not so marked as that seen in the guinea-pigs sensitized to ivy. Of the two, one had been previously painted six and the other nine times. The controls showed no reaction.

COMMENT

The observation that guinea-pigs could be made sensitive to poison ivy confirms the work of Simon and his associates.⁴ It was demonstrated, further, that previous contact as well as a lapse of time is necessary for the production of contact sensitivity. It is apparently much easier to produce sensitivity with poison ivy oil than with other plant oils. The reaction takes place at least from four to six months after the contact is begun and probably much later. This has been shown by Bloch and Steiner-Wourlish,¹ and Simon and his associates,⁴ as well as in this study. It was found that rabbits are not sensitized to poison ivy, nor guinea-pigs to orris root, giant ragweed or sage oils. This has been noted by others.¹⁰ It is difficult to explain why only two of the guinea-pigs tested with dwarf ragweed reacted. Perhaps the technic should have been varied somewhat, or there may be some inherent variation in the animals. It is, at any rate, comparatively easy to sensitize guinea-pigs to poison ivy. Sensitization occurs more regularly with concentrated oil and is more certain to occur the longer the series of original applications. Hence, two of the nine animals painted only three times did not react on subsequent testing. Evidence is also presented that the unsaponifiable fraction of ivy oil contains the active principle of the oil.

CONCLUSIONS

Guinea-pigs were sensitized to poison ivy oil by application to the intact skin.

Rabbits were not similarly sensitized.

Guinea-pigs did not become sensitive to orris root, giant ragweed or sage when treated in this manner.

Two of nine guinea-pigs had definite reactions after previous application of dwarf ragweed oil.

NOTE—Since this paper was submitted for publication two important articles on the subject have appeared, one by Brunsting and Bailey¹¹ and the other by Kobayashi.¹²

10 Simon, F. Personal communication to the author.

11 Brunsting, L. A., and Bailey, R. J. Ragweed (Contact) Dermatitis Produced Experimentally in the Guinea Pig, *J Allergy* 6: 547 (Sept.) 1935.

12 Kobayashi, Y. Sensitization of Guinea-Pigs to *Rhus Vernicifera* and to Japanese and Chinese Lacquers, *Jap J Dermat & Urol* (Abstr Sect) 37: 92 (April) 1935.

ARTERIAL EMBOLISM FOLLOWING INTRAMUSCULAR INJECTION OF A BISMUTH PREPARATION

AARON GROSSMAN, M D

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Bismuth preparations have been used extensively by intramuscular injection for spirocheticidal purposes since 1922. The first instances of arterial embolism were reported before the Schlesische Dermatologische Gesellschaft by Freudenthal¹ in 1923. The literature now contains accounts of some fifty cases, reported mainly from France and Germany. In the United States, Gammel² has noted five, and De Wolf³ two, such accidents. Similar pictures have been observed following the intramuscular injection of mercury, but the pathogenesis had not been understood¹.

REPORT OF A CASE

P. C., a white man aged 38, had begun antisyphilitic treatment seven years previously because of increasing deafness, perforation of the nasal septum and a positive Wassermann reaction of the blood. Since then he had received numerous but irregular courses of treatment with neoarsphenamine and bismuth, the Wassermann reaction of his blood becoming frequently but not consistently negative.

The fifth injection of the present series was given on March 3, 1935, at the inner angle of the upper outer quadrant of the right buttock through a 20 gage 1½ inch (3.75 cm.) needle. It consisted of 1 grain of bismuth subsalicylate suspended in 1 cc. of peanut oil. Aspiration was not attempted. The patient immediately felt severe lancinating pain, which radiated throughout the buttock and down the thigh, but he made no complaint. He was able to walk 1½ miles (2,414 meters) to his home, but then he went to bed because of pain and inability to move the affected limb. The buttock was red, hot, greatly swollen and very tender. The patient felt feverish and was unable to sleep because of his discomfort.

When he was seen on the next day at his home, about seventeen hours after the injection, he appeared to be fairly comfortable. The temperature, pulse, and respiration were normal. The pain was only occasional and not so severe as it was at first. The swelling had gone down, and the redness had disappeared.

From the department of syphilology, service of Dr. Joseph Lebenstein, the Hospital for Joint Diseases.

1 Freudenthal, W. Lokales embolisches Bismogenol-Evanthem, Arch. f. Dermat. u. Syph. **147** 155 (April) 1924.

2 Gammel, J. A. (a) Arterial Embolism. An Unusual Complication Following the Intramuscular Administration of Bismuth, J. A. M. A. **88** 998 (March 26) 1927, (b) Local Accidents Following the Intramuscular Administration of Salts of the Heavy Metals, Arch. Dermat. & Syph. **18** 210 (Aug.) 1928.

3 De Wolf, H. F. Arterial Embolism Complicating Intramuscular Injection of Mercurial and Bismuth Salts, Urol. & Cutan. Rev. **37** 423 (June) 1933.

Covering the buttock was an arborescent violaceous network roughly elliptic and about 8 by 4 inches (20 by 10 cm), which had appeared about eight hours after the onset of the reaction. The skin was hot and exquisitely tender. No nodules could be felt. The limb could be moved spontaneously, but motion was slow and guarded. There were no changes in sensation or reflexes. Two days later he was able to get about.

When he was observed at the clinic ten days after the injection, the patient walked normally. The striae of the lesion had become more livid and were ele-



Appearance of the lesion ten days after the injection of bismuth subsalicylate

vated, cordlike and somewhat warm and tender. Here and there on the network were about eight grayish-black areas, each about $\frac{3}{4}$ inch (1.9 cm) in length. Some of these necrotic spots, according to the patient, had recently discharged yellowish fluid and blood and then dried up. The skin about the mesh was normal in appearance and to palpation except for some new punctate spots (fig).

Twenty days after the injection the network had lost its cordlike feel, was considerably faded and was no longer warm or tender.

Thirty days after the injection the buttock showed only a delicate tracery of fine violet lines. Bismuth subsalicylate was administered intramuscularly near the site of the former injection without any ill effects.

COMMENT

This course is fairly typical of that in the cases of less severe involvement. The marble-like appearance of the lesion is characteristic and has been likened to livedo racemosa or to cutis marmorata, a rare disease of the skin caused by hyperemia of the cutaneous capillaries. In the cases of more severe involvement the condition progresses until gangrene of the skin or of the muscles occurs, so that a large part of the buttock may be involved. A blackish eschar separates, leaving a surface which granulates sluggishly and heals slowly because of the impaired vascularity. In some cases there have been muscular paralyses and sensory changes, probably due to involvement of the nerves through the comitant artery of the sciatic nerve.² In these the recovery of function is slow, may not occur at all and may be followed by trophic ulcers of the foot.^{2b} Embolism through anastomoses of the gluteal and internal pudendal arteries may cause superficial gangrene of the rectum, bladder, vagina,^{2b} vulva, penis, scrotum and thighs.⁴

Early biopsy shows acute inflammatory changes and edema about the affected arteries, which are plugged by emboli of crystals of the bismuth salt used. If a soluble preparation has been employed, the endarteritis induced by caustic action causes thrombosis. Behind the plug the vessels are dilated by a homogeneous mass in which the cellular elements of the blood have decomposed, releasing hemoglobin. Escape of this pigment into the perivascular tissues causes the characteristic violaceous hue. Later, ischemic changes follow this deprivation of blood supply.⁵

Roentgenography,⁶ with proper calibration and exposure, shows a closely meshed plexus, thus proving that not only the visible livid vessels of the skin but also the subdermal vessels are filled with an opaque medium.

Treatment is symptomatic. If there is deep gangrene, surgical intervention⁷ may be resorted to in order to hasten the separation of the slough.

4 Payenneville and Castagnol. Quatre nouveaux cas de dermite livedoïde et gangréneuse de Nicolau à la suite d'injection de Quinby, *Bull Soc franç de dermat et syph* **37** 1027 (July) 1930.

5 Freudenthal¹ Gammel.^{2b}

6 Moncorps, C. Beitrag zur Kenntnis der Embolia cutis medicamentosa nach intramuskularen Bismogenolinjektionen, *Dermat Wchnschr* **95** 976 (July 2) 1932. Merenlender, J. Zur Kenntnis der Embolia cutis arterialis medicamentosa (bismutica), *Arch f Dermat u Syph* **167** 708 (March) 1933.

7 Gougerot, H., and Quénu, J. Traitement chirurgical de la gangrene massive par injection artérielle du bismuth, *Ann d mal ven* **21** 741 (Oct 9) 1926. Martins de Castro, N. Embolie artérielle bismuthique avec lésions graves de la peau l'étude clinique et anatomo-pathologique, *Ann de dermat et syph* **10** 161 (Feb) 1929.

This is a rare accident but not an easy one to avoid. In many of the reported cases aspiration was performed, and though no blood was seen this complication followed. Blood rises slowly through a narrow gage needle and an oily vehicle. Gammel^{2b} offered the best prophylaxis. Aspiration is performed first into a syringe containing saline solution. If no bleeding is noted the syringe is detached and another syringe containing the bismuth preparation is attached to the needle.

PATHOGENESIS OF THE CUTANEOUS COMPLICATIONS OF VARICOSE VEINS

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The pathogenesis of the cutaneous complications of varicose veins is usually explained on the basis of chronic passive congestion of the skin and of the subcutaneous tissues, which results from venous stasis in the varicose superficial vessels. Many of the clinical features of these complications, however, are not compatible with this explanation and support, rather, the interpretation, expressed in previous publications,¹ that the cutaneous lesions are of inflammatory origin, arising by extension from phlebitis of the varicose veins. One of the principal arguments in favor of this hypothesis is the topographic relationship between the cutaneous lesions and the varicose trunks.

Attention has been called to the value of infra-red photography² for visualizing subcutaneous varicosities. By means of this method it is possible to demonstrate an immediate topographic association of varicose eczema and ulcer with subjacent dilated trunks. In the accompanying illustrations are seen various types of cutaneous lesions associated with varicose veins. The infra-red photographs of the same limbs show the distribution of the varices. In each of the pairs of photographs it may be seen that immediately beneath the cutaneous lesion there is a dilated venous trunk or pool. This topographic proximity of cutaneous lesions and varicose trunks speaks convincingly against stasis as the cause of the cutaneous condition. If stasis resulted from such a varicosity, it would be in the tissues about the capillary bed which drains into the varicose vein and not in the skin overlying

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1 Zimmerman, L. M. Complications and Treatment of Varicose Veins, *Illinois M J* **59** 60 (Jan) 1931. Phlebitis, Thrombosis, and Thrombophlebitis of the Lower Extremities, *Surg, Gynec & Obst* **61** 443 (Oct) 1935.

2 Zimmerman, L. M., and Rattner, H. Infra-Red Photography of Subcutaneous Veins, *Am J Surg* **27** 502 (March) 1935.

the trunk itself. Direct pressure of the varix on the adjacent skin might be mentioned as a factor, but comparable cutaneous lesions do not occur elsewhere over soft tumors or other pressure points.

The topographic relation between the vein and the cutaneous lesion confirms the belief that the complications of varicose veins are of inflammatory origin and that a direct sequence of events can be traced from the varicose vein to the final lesion. The first step in the chain

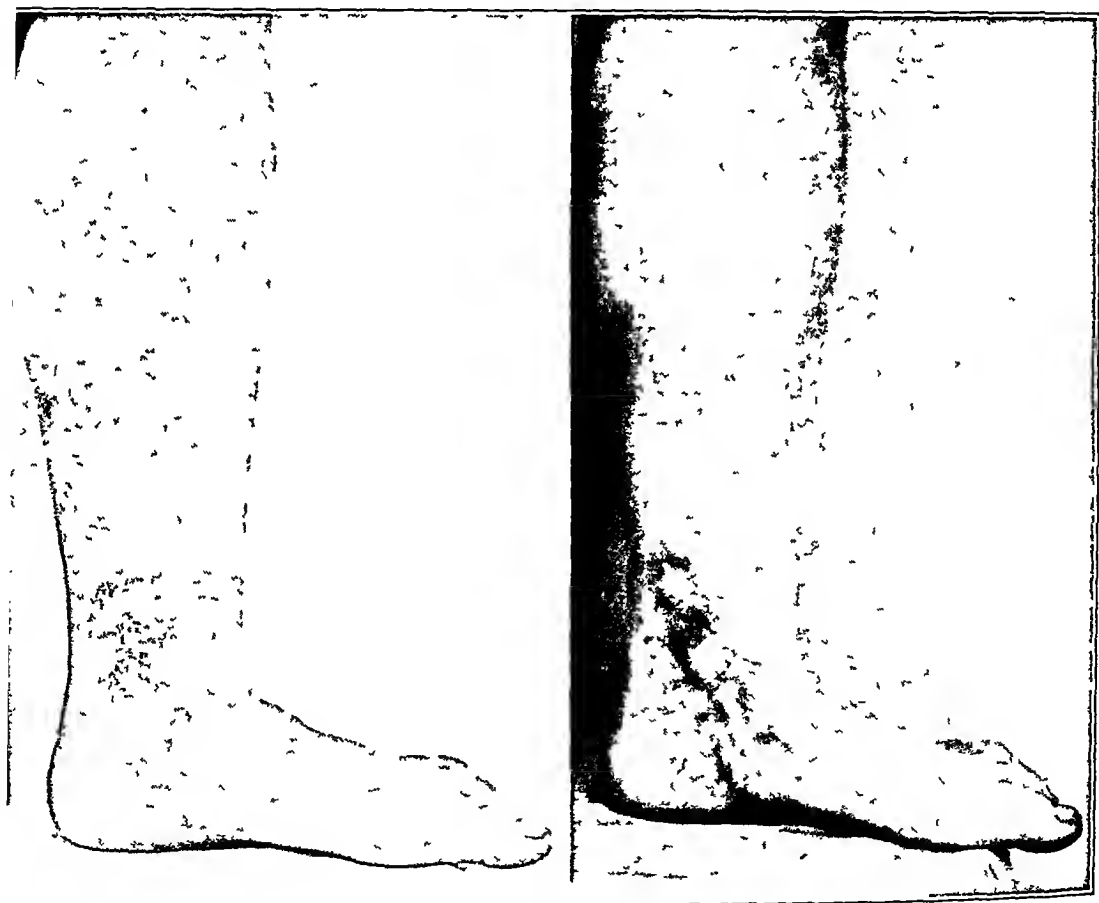


Fig 1 (A H, a woman aged 38) —The patient had a "phlebitic ulcer" five years before the photographs were taken. The conventional photograph shows a pigmented, indurated scar above the internal malleolus and an indurated "plaque" in the middle third of the leg. The infra-red photograph shows a network of varicose veins immediately beneath both the scar and the induration.

is phlebitis, which constitutes the most common complication of varicose veins. The frequency of phlebitis is explained by the stasis and anoxemia within the vessel and the changes in the intima, all of which

predispose to the localization of blood-borne organisms. These organisms reach the vessels from focal or intercurrent infections, and may remain inactive between successive attacks of inflammation. As a result of recurring localized phlebitis, the inflammation extends to the adjacent skin and subcutaneous tissues and a patch of subacute cellulitis appears.

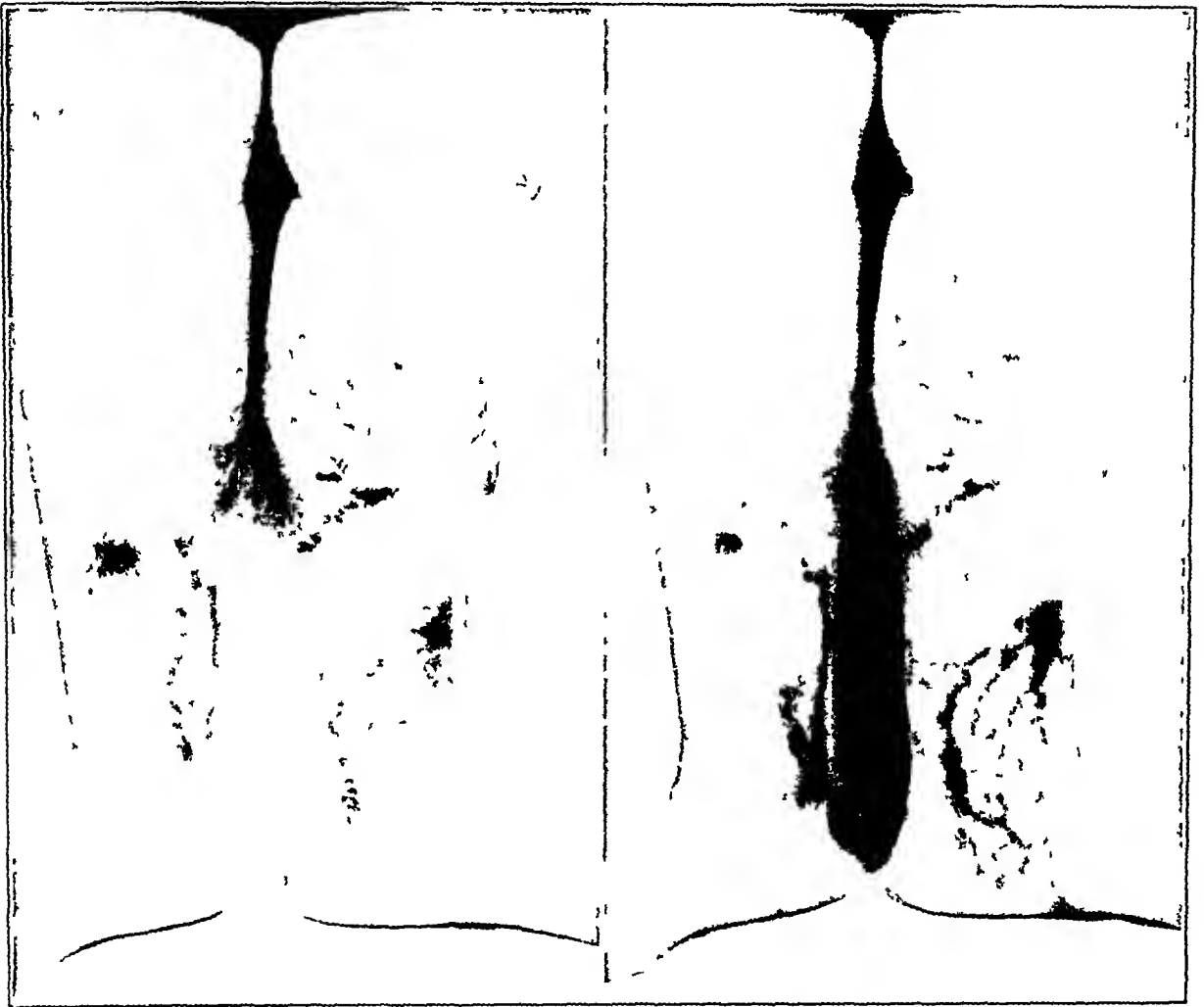


Fig 2 (H K, a woman aged 40) —Old phlebitis of the deep veins was followed by inflammation of the superficial veins. The conventional photograph shows pigmented areas on both legs and extensive scarring on the inner aspect of the left ankle. The infra-red photograph shows the coincidence of distribution of varices and cutaneous involvement.

With repeated recurrence and subsidence of these attacks of cellulitis, permanent irreversible changes take place, including pigmentation, infiltration, cicatrization, atrophy and adherence of the integument to the

deeper structures Superimposed on these changes are the eczemas, induration, dermatoses and ulcers, representing the end-stages of this inflammatory sequence



Fig 3 (N J, a woman aged 42) —The patient had old puerperal phlebitis and a healed varicose ulcer The infra-red photograph shows large varicose pools immediately in the center of the indurated zone, beneath the scar of the ulcer

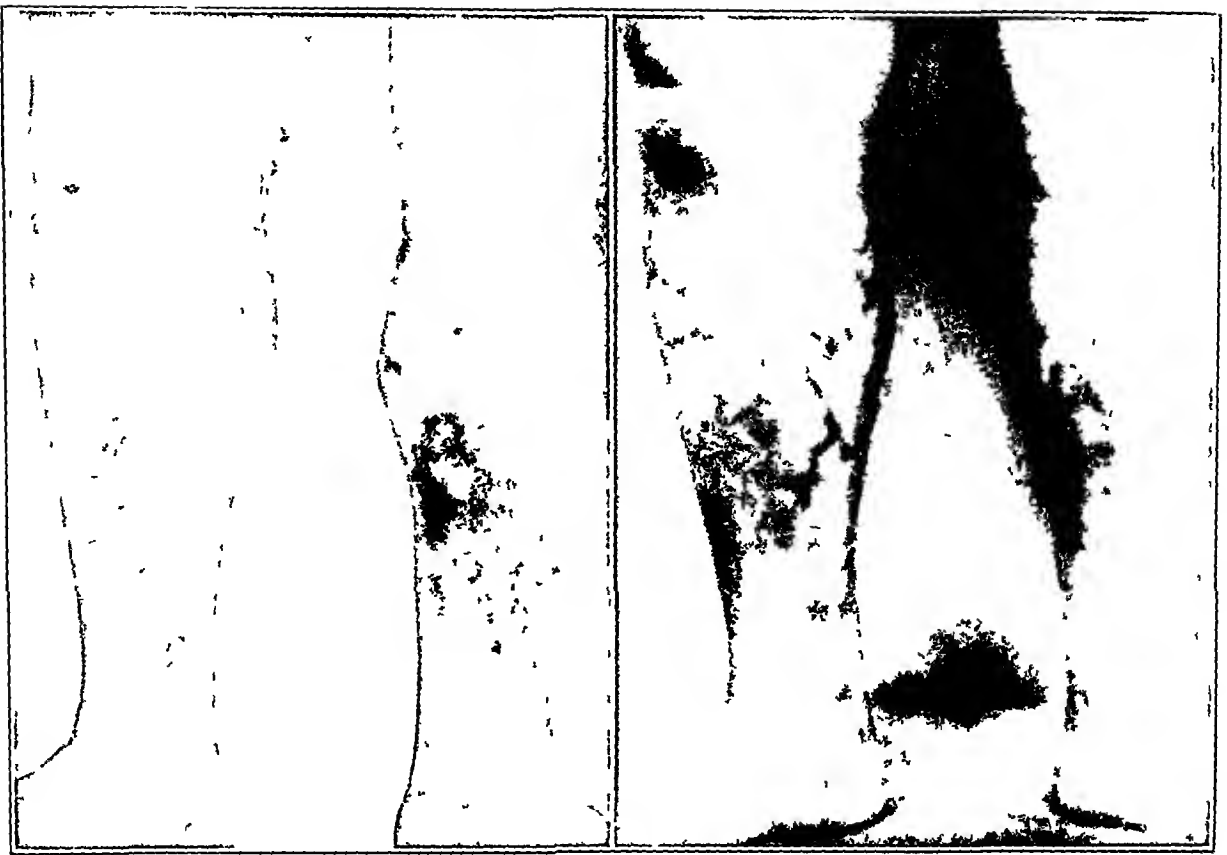


Fig 4 (F P, a woman aged 45) —The patient had eczema, induration and discoloration of both legs. The photographs show the topographic coincidence of veins and cutaneous lesions and the absence of varicosities below the pigmented areas



Fig 5 (C L, a woman, aged 75) —The patient had eczema, with beginning ulceration and large varicosities subsequent to the lesion which is not in the most dependent portion of the leg

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SUMMARY

Infra-red photographs of varicose veins and their cutaneous complications reveal an immediate topographic relationship between the dilated trunks and the overlying cutaneous lesions. This is offered as further proof of the contention that these cutaneous lesions are not the result of chronic passive congestion, as is usually stated, but are

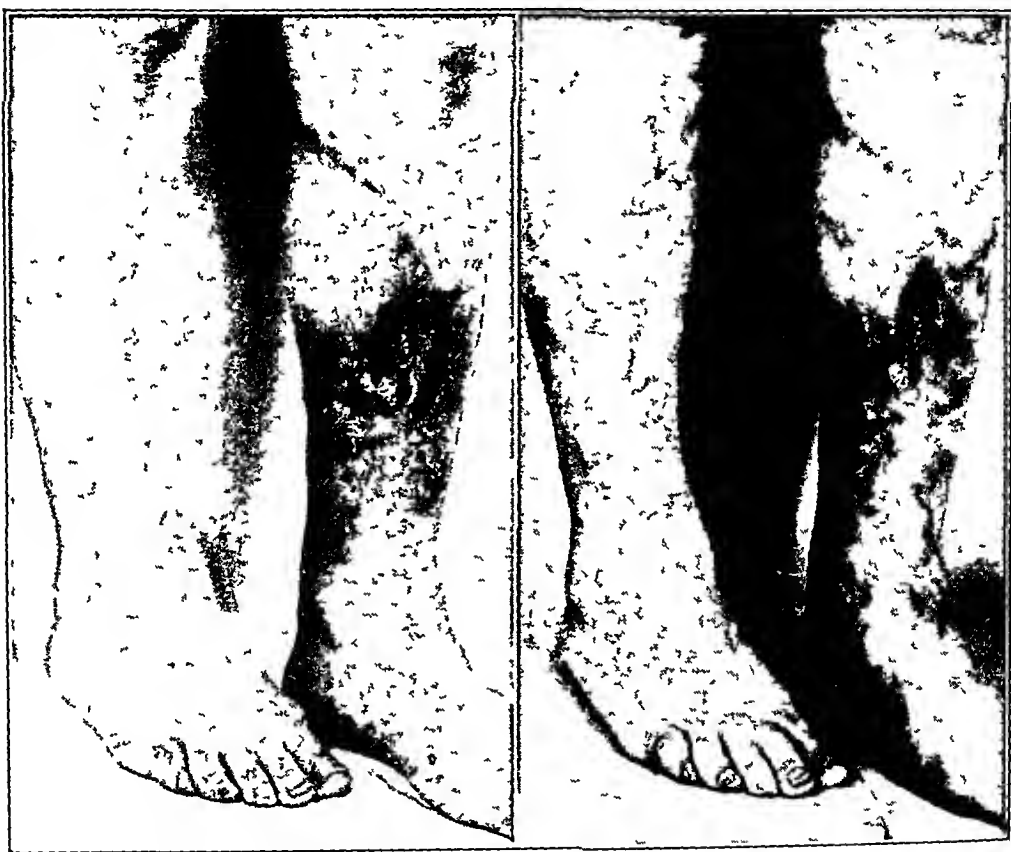


Fig 6 (W C, a woman aged 45) —A large deep callous ulcer is seen near the middle of the left leg, and there is induration of both legs. Note the absence of varices on the anterior aspect of the left leg, corresponding to the area of relatively intact skin.

of inflammatory origin, arising by direct extension from infections within the varicosities.

Miss Madge Walsh, of the department of photography of the Northwestern University Medical School, assisted in preparing the photographs.

FIXED ARSENICAL ERUPTION

SENSITIVITY TO TRYPARSAMIDE AT SITES OF PIGMENTATION FOLLOWING DERMATITIS DUE TO SILVER ARSPHENAMINE

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PHILADELPHIA

The occurrence of a fixed eruption due to tryparsamide is a rare complication of antisyphilitic treatment, the case reported by Robinson¹ being the only one on record. For some time I have had under observation a patient in whom sensitivity to tryparsamide developed at the sites of pigmentation which remained after arsphenamine dermatitis sustained four years previously. It was found that the patient was sensitive to all trivalent arsenicals over the entire cutaneous surface, as evidenced by patch and intradermal tests, and to tryparsamide only in the pigmented areas.

REPORT OF CASE

W. Y., a white man aged 40 years, was first seen in June 1933, when he requested continuation of antisyphilitic treatment. He stated that he had a penile lesion in 1919, which healed in five or six weeks. No secondary lesions were noted and no treatment was given. In 1925 he became depressed and nervous. The Wassermann reaction of his blood was positive, and treatment with neoarsphenamine was started. Symptomatic response was good, and no reaction to treatment was noted until 1929. Between 1925 and 1931 the patient received approximately thirty injections of neoarsphenamine, twenty of silver arsphenamine, fifty of a bismuth preparation and fifty of an insoluble preparation of mercury.

In 1929 he noted some itching and a patchy dermatitis of the hands, face and upper part of the trunk after each injection of arsphenamine. After an injection of 0.2 Gm. of silver arsphenamine he had fairly severe generalized dermatitis with exfoliation, which lasted for from three to four weeks. There remained pigmented macules of varying sizes over the arms, upper part of the trunk, face and neck, many of them at the sites of the patchy dermatitis. From 1929 to 1932 alternate courses of tryparsamide and heavy metal were given. When I first saw the patient he had received approximately thirty-five injections of tryparsamide. After the last six or eight he had noted some edema and livid erythema, with moderate itching, at the sites of the pigmented macules.

The Wassermann reaction of the blood had been negative since 1927. The patient had never permitted an examination of the spinal fluid to be made. It is certain that no tryparsamide was administered before the attack of arsphenamine dermatitis.

From the Department of Dermatology and Syphilology, University of Pennsylvania School of Medicine. Dr. John H. Stokes, Director.

¹ Robinson H. M. Fixed Dermatitis Due to Tryparsamide, *Am. J. Syph. & Neurol.* 17:507 (Oct.) 1933.

Physical Examination—The patient was a flabby, asthenic person looking considerably older than the stated age. Bluish-brown macules varying in size from 1 to 4 cm were scattered over the skin of the arms, trunk, neck and face. The macules were round or ovoid and sharply margined. The mucous membranes showed no pigmentation. Except in regard to the central nervous system, the rest of the examination gave negative results. The positive neurologic findings included sluggish and incomplete reaction of the pupils to light, hyperactive, bilaterally equal tendon reflexes, moderate slurring of the test phrases and some loss of memory. The reaction to questioning and examination was alert. The patient showed marked introspective tendencies and a surprising knowledge of methods of antisyphilitic treatment. The Wassermann and Kahn reactions of the blood were repeatedly negative. Examination of the spinal fluid in August 1934 gave negative results with all four standard tests.

Further Course—Tryparsamide therapy was continued, with observation of the skin a day or two after each injection. A syringe free from arsphenamine was used. Within from twelve to fifteen hours after each injection there developed at the site of the fixed eruption an urticarial reaction and a purplish erythema exactly simulating that seen in phenolphthalein eruption. Ingestion of phenolphthalein produced no effect on the skin. With succeeding injections of tryparsamide the local reaction became more pronounced and the patient complained of mild general malaise and drowsiness. After having received thirteen injections he refused further intravenous therapy. A distinct variation in the reactions of the skin to 1 Gm and to 3 Gm of tryparsamide was noted, the reactions to the larger amount being much more marked.

Results of Patch and Intradermal Tests with Tryparsamide, Neosalphenamine, Silver Arsphenamine, Bismarsen and Sodium Bismuth Tartrate—All the arsphenamines used produced a definitely positive reaction to patch tests (sharp erythema and vesicles) within twenty-four hours on the normal skin and at the sites of pigmentation. The reaction in both areas was sharply localized to the portion of skin in contact with the gauze soaked in the testing material (30 per cent solution). In the intradermal tests on pigmented areas there was a tendency for the entire area to react, but the reaction about the site of the injection was much more marked. Patch and intradermal tests with a 30 per cent solution of tryparsamide produced no reaction on the normal skin, at the sites of pigmentation there occurred a reaction exactly like that seen after an intravenous injection of tryparsamide, edema and purplish erythema appearing evenly in the entire macule, with no extension to the surrounding normal skin. Examination with a lens revealed no vesicles, and the immediate site of contact with gauze soaked with tryparsamide could not be made out. The reaction developed more slowly than with the arsphenamines and did not begin to subside until forty-eight hours after the removal of the patch. There was no reaction to patch or intradermal tests with a 10 per cent concentration of soluble sodium bismuth tartrate.

Biopsy—A portion of one of the pigmented patches was removed four weeks after the administration of 3 Gm of tryparsamide intravenously, no gross evidence of the reaction being present. Fixation and staining were by the routine formaldehyde and hematoxylin-eosin method. The epiderm was somewhat thin and there was considerable pigment in the basal layers. There was no spongiosis or intradermal formation of vesicles. The outstanding changes were in the papillae and upper portion of the corium, which showed marked edema, a sparse round cell infiltrate and numerous chromatophores. The appendages were normal.

Biospectrometric Analysis (Dr L. Edward Gaul, New York) —Analysis was made of a portion of the skin fixed with formaldehyde. The metallic elements in the specimen were present in normal quantities with the exception of lead and manganese, the density of the lead line indicating 1 plus retention and that of the manganese line a slight excess. The significance of the slight excess of manganese was not apparent, and the possibility of contamination from the formaldehyde was considered. It is to be noted especially that there was no retention of silver or arsenic, indicating that no local fixation of tryparsamide had taken place.

COMMENT

The significant findings in the case may be outlined as follows: (1) a fixed macular pigmentation persisting after an exfoliative dermatitis due to silver arsphenamine, (2) a livid, erythematous urticarial reaction which developed gradually and became increasingly severe after successive injections of tryparsamide, (3) eventual complaint of general malaise and drowsiness, (4) universal sensitivity of the entire skin to arsphenamines, as evidenced by positive reactions to patch and intradermal tests, and (5) sensitivity to tryparsamide localized at the sites of the fixed eruption.

In the case of fixed eruption due to tryparsamide reported by Robinson,¹ patch tests with tryparsamide on both the involved and the uninvolved skin gave negative results. This is not surprising, as fixed eruptions due to drugs are markedly capricious in this regard.² An analogous case has been reported by Gougerot and Boudin,³ in which erythroderma of the hands and feet was produced by injections of acetylarsan, a pentavalent arsenical, nine years after generalized erythroderma due to neoarsphenamine, a trivalent arsenical. In this case apparent universal sensitivity to acetylarsen was present, as evidenced by patch tests. The eruption was not fixed, in the usual sense.

I believe that the distinctly different types of reaction to arsphenamine and tryparsamide seen in the patch tests in my case are worthy of an attempt at interpretation. The reaction to arsphenamine was of the eczematous type, superficial and sharply limited to the portion of the skin in direct contact with the allergen. It developed rapidly and started to subside as soon as the patch was removed. The reaction to tryparsamide developed more slowly (in forty-eight hours) and persisted unabated for two days after removal of the patch. It was not superficial and was distinctly not limited to the site of the contact with tryparsamide, and there was no vesicle formation. It seems entirely possible that the reaction developed as a consequence of absorption of the tryparsamide, since the site of shock tissue was principally in the

2 Sulzberger, M. B., Wise, F., and Wolf, J. A Tentative Classification of Allergic Dermatoses, *J. A. M. A.* 104:1489 (April 27) 1935.

3 Gougerot, H., and Boudin, G. Erythrodermie arsenicale localisée aux mains et aux pieds, *Ann. d. mal. ven.* 29:240 (June) 1934.

upper portion of the cutis, the superficial portion of the epiderm remaining grossly unaffected by the passage of the drug through it. The classification of allergic dermatoses, recently advanced by Sulzberger, Wise, and Wolf,² is based on the site of the shock tissue, the reaction time, the characteristic lesion and pathologic process, and the type of diagnostic test most suitable. The reaction of my patient to arsphenamine belongs to type I of this classification, eczematous reactions in which the site of the shock tissue is the epiderm, though perhaps originally to type IV, miscellaneous reactions, including fixed drug eruptions. The reaction to tryparsamide was of type IV.

It seems not improbable that in the original sensitivity to arsphenamine both the epiderm, with its exfoliative dermatitis, and portions of the cutis, with their fixed eruption and pigmentation, were the sites of shock tissue, and that the gradually developing sensitivity to tryparsamide manifested itself in the portions of the cutis which were previously the shock sites for arsphenamine. One may speculate as to whether or not the patient would have had a fixed tryparsamide eruption had not the previous heterophile sensitization with arsphenamine occurred. The fact that no previously unaffected sites became the seat of the tryparsamide eruption is significant. This may indeed be another example of the Sanarelli phenomenon⁴ as applied to the skin, in which previous sensitization to a heterophile substance leads to reaction at the affected site to a large variety of normally nontoxic substances.⁵

SUMMARY

A case is reported of a fixed eruption due to tryparsamide occurring only at the sites of pigmentation following an arsphenamine eruption sustained four years previously. The possible significance of this superimposed sensitivity, with the cutis as the site of shock tissue, is briefly discussed.

4 Sanarelli, G. Le cholera experimental, *Ann Inst Pasteur* **38** 11, 1924.

5 The Synergistic Etiology of Poliomyelitis, editorial, *J A M A* **103** 757 (Sept 8) 1934.

EXPERIMENTAL ARSPHENAMINE DERMATITIS

REACTION TO ARSPHENAMINE IN NORMAL GUINEA-PIGS AND IN GUINEA-PIGS GIVEN STAPHYLOCOCCUS TOXIN

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In a previous communication ¹ certain preliminary observations were made on the nature of arsphenamine ² dermatitis as produced in guinea-pigs

It was noted that sensitization to arsphenamine was easily produced in the guinea-pigs used in this experiment. Two brands of arsphenamine were used. It was further noted that different brands of neoarsphenamine and different lots of the same brand of arsphenamine varied greatly in their power to cause cutaneous sensitization of normal guinea-pigs fed a diet high in vitamin C. Furthermore, the degree of sensitivity developed seemed higher when a single lot of arsphenamine of a high sensitizing index was used throughout the sensitizing period. A considerable variation in reactivity was encountered when a subsequent injection of arsphenamine was given intravenously. When the second "sensitizing" intradermal injection was made with two different brands of arsphenamine and the subsequent intravenous injection was made with that brand of arsphenamine which had been used both for the preliminary and for one of the second sensitizing injections, the focal reactions were distinctly more frequent and more severe in the area in which the same brand of arsphenamine had been given intradermally. When a different brand of neoarsphenamine was used for the intravenous testing, the reactions were less frequent and less marked. This, of course, suggested that sensitization may be confined more or less to the individual brand of arsphenamine causing the sensitization. It also suggested that intravenous testing in human beings in whom the second sensitizing injection is apparently not necessary to produce dermatitis,

From the section on Dermatology, Department of Medicine, Royal Victoria Hospital

1 Cormia, F E. Experimental Arsphenamine Dermatitis. I. Canad M A J **34** 272 (March) 1936

2 The terms arsphenamine and neoarsphenamine are used interchangeably throughout this report, neoarsphenamine however, was the official drug used in each experiment

may be superior to the intradermal test recently partially discredited. This confirms the similar statement made by Moore and his co-workers³ on the clinical value of intravenous testing.

The localized nature of the reactivity in guinea-pigs to the intravenous injections of arsphenamine further indicated that a disturbance in local cellular equilibrium had been caused by the direct action of the arsphenamine solution. It was inferred that this was in part due to local injury to the tissue, since vascularly administered arsphenamine gave rise to a cutaneous flare only when the intravenous injection was preceded by two intradermal injections. In the present paper further observations are made on the nature of experimental arsphenamine dermatitis in guinea-pigs.

REACTION TO ARSPHENAMINE IN NORMAL GUINEA-PIGS

EXPERIMENT 1—Two groups of guinea-pigs were given injections of a single brand of arsphenamine, the two methods of injection of the previous experiment and that outlined by Sulzberger⁴ being used. The arsphenamine was injected into an initial group of seven normal guinea-pigs and into a second group of six normal guinea-pigs procured from the same source one month after the first group. Of the first group of seven guinea-pigs, six were definitely sensitized, there being three 3 plus reactions, two 2 plus and one 1 plus. Of the second group of six guinea-pigs, but three reacted, there being two 2 plus reactions and one 1 plus reaction.^{4a}

From experiment 1 the following conclusion was drawn. Different groups of guinea-pigs present considerable variations in the ability to become sensitized, these variations being independent of the diet and of the type of arsphenamine injected.

EXPERIMENT 2—Six guinea-pigs were given injections of brand "A" of arsphenamine, twelve months old. Another six were given injections of brand "A" of arsphenamine, six months old. Five of the first six showed positive sensitization reactions. In the second group only three of the six animals reacted positively.

The conclusion was drawn that the age of the preparation may possibly be a factor in the ability to produce sensitization to arsphenamine in guinea-pigs.

3 Moore, J. E., Woo, S., Robinson, H., and Gary, S. Reactions of the Skin Following the Intradermal Injection of Arsphenamine. Postarsphenamine Dermatitis, *Arch Dermat & Syph* **23** 74 (Jan.) 1931. Robinson, H. Patch Tests in Determination of Arsphenamine Sensitization, *South M J* **27** 845 (Oct) 1934.

4 Sulzberger, M. B. Hypersensitiveness to Arsphenamine in Guinea-Pigs. I. Experiments in Prevention and in Desensitization, *Arch Dermat & Syph* **20** 669 (Nov.) 1929.

4a Reactions were tabulated as 1 plus when the area of erythema was 1 cm in diameter, 2 plus when it was 2 cm in diameter, 3 plus when it was the size of a quarter with or without a small central area of edema and 4 plus when it was the size of a silver dollar or larger, with a large area of central edema.

REACTION TO ARSPHENAMINE IN GUINEA-PIGS GIVEN
STAPHYLOCOCCUS TOXIN

The recent experimental work of Burky⁵ suggested that certain products of infection effect changes in the organism which act as an adjunct in the production of sensitization

Burky was able, by the simultaneous use of a highly powerful staphylococcus toxin, to sensitize rabbits to rabbit lens, a hitherto impossible procedure. The principles underlying this experiment are unknown, on the basis of innumerable clinical observations the products of infection are supposed to broaden the base of sensitivity. Burky had previously noted that immunity can be produced in rabbits by the intradermal injection of staphylococcus toxin. In the course of this experiment he accidentally observed that while an initial immunity to the toxin developed in the rabbits, continued injections caused increased reactions. This was subsequently found to be due to sensitivity to the broth in which the toxin was suspended and led to the later experiment with rabbit lens.

On the basis of this work it seemed expedient to determine, if possible, the effect of staphylococcus toxin in the production of cutaneous hypersensitivity to arspenamine in guinea-pigs.

A preliminary group of control experiments were performed to determine the nature of the action of staphylococcus toxin. The Burnet toxin, prepared under the supervision of Dr. E. G. Murray, professor of bacteriology at McGill University, was used throughout. The toxin was kept at a constant level, about 7,000 Burnet units.

EXPERIMENT 1—Four young adult guinea-pigs were given intradermal injections once weekly for six weeks of 0.1 cc of the sterile filtered broth medium, in which the toxin was suspended for the first experiment. There were no cutaneous reactions to any of the injections.

Standardization of the action of the toxin in a series of twelve normal guinea-pigs was carried out as follows: various amounts of the toxin, from 0.1 cc to 0.000005 cc, were injected intradermally into the abdomens of normal guinea-pigs once weekly for six weeks. A characteristic type of lesion was observed. A small dose, 0.001 cc or less, resulted in the formation of a small inflammatory papule. When 0.001 cc or more was given, a small necrotic central area also developed. Large doses (0.001 to 0.1 cc) caused one of two types of lesion: (1) a hemorrhagic center with surrounding necrosis and a vivid red border of inflammation (with the largest doses there was an accompanying edema, later the large necrotic area became crust-covered and adherent to the underlying muscle tissue) or (2) a large central area of hemorrhagic necrosis with a faint grayish periphery and a surrounding pinkish inflammatory halo.

⁵ Burky, E. Studies on Cultures and Broth Filtrates of Staphylococci. I, II and III, *J. Immunol.* 24:93, 115 and 127 (Feb.) 1933. Studies on Cultures and Broth Filtrates of Staphylococci. IV. Antitoxin Content of Rabbit Serums Immune to Staphylococcus Toxin and Precipitin Reactions to Such Serums, *ibid.* 25:419 (Nov.) 1933. Production in Rabbit of Hypersensitive Reactions to Lens, Rabbit Muscle and Low Ragweed Extracts by Action of Staphylococcus Toxin, *J. Allergy* 5:466 (July) 1934.

In seven of the twelve guinea-pigs the reactions of the skin to successive injections became more marked. This was noted particularly after the third and fourth injections. The later reactions were from one and one-half to two and one-half times as large as those of the initial injections. This occurred despite the fact that the same batch of toxin was used throughout, i e., a toxin of diminishing strength. The strength of the toxin diminished so rapidly that after four weeks the size of the lesion produced by the initial injection in a series of three control animals was but half that of the lesion produced by the reaction to fresh toxin. Of the seven guinea-pigs which showed increased reactions to toxin of diminishing strength, four were included in the group of five which died of toxemia. All these seven guinea-pigs had injections of 0.005 cc or over. The optimum concentration of toxin necessary to produce increasing reactions was from 0.01 to 0.05 cc.

For four of the seven animals with increasing reactions it was possible to give a subsequent control injection of 0.1 cc of the filtrate from beef heart-peptone agar broth. In each instance a papule (from 4 to 12 mm in diameter) appeared. In one instance a hemorrhagic center developed, and in another there was a small central area of necrosis. This experiment seems to indicate that the guinea-pigs had become slightly sensitive to the agar broth, since no reactions occurred when the broth was injected into animals of a control series.

The larger doses of toxin caused a general toxemia (chiefly vasculotoxic) and loss of weight. These guinea-pigs were also subject to pneumonia, three dying of toxemia, with multiple subcutaneous and visceral hemorrhages, two of toxemia and pneumonia and three of pneumonia.

Five cubic centimeters of blood was withdrawn from the heart of two of the guinea-pigs to determine the amount of antitoxin produced. In the first animal, which had received six injections of toxin, each of 0.001 cc, there developed 1,000 Burnet antihemolytic units of antitoxin. In the second guinea-pig, which was given similar injections but with a weekly dose of only 0.00005 cc, there developed less than 250 units of antitoxin (a negligible amount).

To determine the toxicity of the toxin two normal guinea-pigs were given intravenous injections of fresh toxin, the first of 0.01 cc and the second of 0.001 cc. Both died within forty-five seconds.

In conclusion, the Burnet toxin is highly lethal for guinea-pigs. It causes characteristic reactions when injected intradermally, which are not reactions to the broth per se, but which may be increased reactions to the broth due to some unknown action of the toxin on the skin in particular and on the immunity mechanism of the body in general. When proper dosage is used, antitoxin in appreciable amounts can be demonstrated in the blood of guinea-pigs. A marked toxemia results when the injections are continued over a period of weeks. The toxin is vascularly toxic, causing a hemorrhagic necrosis in situ and distal hemorrhages in both the subcutaneous tissue and the viscera and rapidly causing death when given intravenously. The reaction is apparently similar to that occurring in rabbits,⁶ since there was a marked pulmonary engorgement and resultant failure of the right side of the heart.

6 Kellaway, C. H., Burnet, F. M., and Williams, F. E. *The Pharmacological Action of the Exotoxin of Staphylococcus Aureus*, *J. Path. & Bact.* **33**: 889 (Oct.) 1930.

EXPERIMENT 2—This experiment was made to determine the results of the simultaneous injection of the Burnet staphylococcus toxin and neoarsphenamine in guinea-pigs

Five-hundredths cubic centimeter of a 7,000 unit⁷ standard Burnet toxin was mixed with 0.1 cc of a solution of neoarsphenamine prepared as in the previous experiments and containing 0.00015 Gm of neoarsphenamine. This mixture was immediately injected intradermally into the depilated abdomen of a guinea-pig.

The method used by Burky was attempted but was not feasible. This consisted of adding to the freshly inoculated agar broth culture of staphylococci neoarsphenamine in sufficient quantity to make a 1:1,000 solution. Unfortunately, the aerobic conditions necessary for bacterial growth rapidly oxidized the neoarsphenamine. In addition, the concentration of the arsphenamine preparation required completely prevented the growth of the staphylococcus.

Eighteen normal guinea-pigs were selected for the experiment. In addition, sixteen from previous experiments were used to determine the effect, if any, of the toxin-arsphenamine mixture on preexisting sensitization.

Group 1—This group consisted of three normal guinea-pigs and four others in which previous attempts to produce sensitization were unsuccessful, i. e., which could not be sensitized intradermally by the two injection method.

During the first week the toxin-arsphenamine mixture was given, then the toxin was injected alone once weekly for three injections, and then the neoarsphenamine was injected alone after one more week.

The reaction to the initial injection was an area of hemorrhage and edema the size of a quarter, with a small central area of necrosis. The following week similar-sized lesions were produced with the toxin alone, and the previously resistant guinea-pigs reacted also with a slight to moderate degree of erythema in the area in which sensitization with neoarsphenamine had been previously attempted. However, the next two weekly injections of toxin produced gradually diminishing reactions, and when the test dose of neoarsphenamine was given after another week no reactions were observed. The conclusion was drawn that the toxin did not have a definite sensitizing effect in previously unsensitizable guinea-pigs, in fact it seemed as if some other factor had intervened, since the three normal guinea-pigs could not be sensitized by the toxin-arsphenamine method.

Group 2—This group consisted of five guinea-pigs which had shown weak sensitization reactions in previous attempts to produce sensitization. The method used was that used in group 1. The initial reactions were lesions the size of a quarter similar to those described for group 1. The following week the toxin alone was given, but in two guinea-pigs, in addition to the hemorrhagic and edematous local reaction to the toxin, markedly erythematous and edematous flares developed in the area of sensitization of the previous experiment. In a third guinea-pig in this series there developed a slight erythema. The subsequent history was one of diminishing reactions to the two last injections of toxin and a single 1 plus papular reaction to the last dose of neoarsphenamine.

The conclusion seemed justified that after the early flare-ups in the sites of previous sensitization there was an actual decrease rather than an increase in dermal sensitivity.

Group 3—The group consisted of four guinea-pigs which had shown strongly positive sensitization reactions in the earlier experiments.

The method was that used for group 1.

⁷ One cubic centimeter of a 1:7,000 dilution of toxin causes 50 per cent hemolysis in 0.1 cc of a 10 per cent suspension of rabbit cells.

The local reactions to the toxin-arsphenamine mixture and to the toxin were comparable to those in group 2. After the first injection of the toxin (alone), however, a marked erythema and some edema appeared over the remainder of the abdomen and particularly over that part into which the arsphenamine was injected in the previous experiment. In the other two guinea-pigs a less marked erythema appeared. These lesions subsided within two days.

The subsequent history in group 3 was one of diminishing reactions to the toxin, and when the test dose of neoarsphenamine was given there was but a small papular reaction in each guinea-pig. Here again the conclusion was drawn that after the early, possibly idiosyncratic, reactions, immunity developed to the toxin and that the degree of sensitization to the neoarsphenamine had greatly decreased during the experiment.

Group 4—Twelve normal guinea-pigs were given toxin and neoarsphenamine with the technic outlined for group 1.

These guinea-pigs had increasing reactions to the first three of the injections and then decreasing reactions. The reactions to the test dose of neoarsphenamine



Included in the photograph are one of the guinea-pigs from group 2 and one from group 3. The thick, dark crusts on the right side of the abdomen represent the involuting reaction to the initial injection, the acute hemorrhagic and edematous lesions on the left side of the abdomen represent the reactions to the toxin alone, while within the broken lines the erythematous and slightly edematous flares can be clearly seen.

were small, and only seven of the twelve guinea-pigs reacted. The reactions produced small papules in every instance, in but one animal was there a surrounding erythematous flare the size of a nickel.

Toxin exhibited no significant effect in the cutaneous sensitization to neoarsphenamine in normal guinea-pigs.

Group 5—This group of six normal guinea-pigs were given injections after the method suggested by Burky and with the knowledge that, according to Sulzberger,⁴ sensitization would not occur. The toxin was mixed with the neoarsphenamine in the usual dosage and was injected intradermally at weekly intervals for five weeks.

Increasing local reactions were obtained to the first three injections and decreasing reactions to the last two. When the test dose of neoarsphenamine was given

alone, this group showed the fewest and the least marked reactions in the entire series. Only three of the six reacted, and these with minute papules.

No sensitization to neoarsphenamine was produced.

COMMENT

Further experiments are now being made both with the animals previously used and with a new series of guinea-pigs. It is obviously impossible to draw conclusions from so small a group, and the experiment will be carried on throughout the year, various methods and different controls being used.

It is apparent that there was a curious decrease in sensitivity in the previously sensitized guinea-pigs throughout the experiment. Normal animals proved resistant to a brand of neoarsphenamine which in the earlier experiments was given a high sensitizing index. The addition of the highly potent toxin did not, with the exception of the early flare-up of old lesions, seem to have any augmenting influence in the production of hypersensitivity. The entire experiment suggested that some unknown factor was at work inhibiting the development of cutaneous arsenical idiosyncrasy.

The time of the experiment was from May 20 to July 5, and during that time the diet was kept constant, with large amounts of vitamin C. There may have been a slight increase in the amount of available sunlight, but this must have exerted a minor influence.

It is possible that sensitization to arsphenamine in guinea-pigs may, like allergy to tuberculin in human beings, undergo waves and changes with the seasons. In addition, different groups of guinea-pigs react differently even when the environment is a constant factor. The variation in the degree of sensitivity in a single group of guinea-pigs was another striking phenomenon.

Practically all dermatologists and syphilologists have noted the influence of infection on idiosyncratic and hyperallergic types of cutaneous eruption. The influence of intertriginous mycoses on the course of arsphenamine dermatitis has recently been commented on by Stokes and Kulchar.⁸ It would appear that infections do predispose the organism to various idiosyncratic upsets and broaden the bases of existing allergies. The mechanism of this phenomenon is unknown. Burky⁹ was under the impression that toxin has a general sensitizing influence which is intimately bound up with the production of specific hyperallergy and immunity. Hooker,¹⁰ on the other hand, believed that

8 Stokes, J. H., and Kulchar, G. Infection-Allergic Complex in Arsphenamine Dermatitic Reactions with Special Reference to Dermatophytosis, *Brit J Dermat* 46 134 (March) 1934.

9 Personal communication to the author.

10 Personal communication to the author.

the action of the toxin is purely a locally irritating one and that any cutaneous irritant will serve the same purpose. The results of certain of the earlier experiments with guinea-pigs¹ have tended to confirm the latter impression.

CONCLUSIONS

Different groups of guinea-pigs exhibited considerable variations in their ability to become sensitized to neoarsphenamine, these variations being independent of diet and of the brand of neoarsphenamine injected.

The age of the arsenical preparation may be a factor in the production of cutaneous hypersensitivity.

The Burnet staphylococcus toxin is highly lethal for guinea-pigs.

Continued injections of toxin intradermally in guinea-pigs produced increasing reactions, which indicated in part a developing sensitivity to the agar broth.

A degree of active immunity to staphylococcus toxin could apparently be developed in guinea-pigs.

The early injections of toxin seemed to activate the sites of old lesions due to arsphenamine.

Toxin (in this series) played no significant part in the production of cutaneous hyperallergy to neoarsphenamine in guinea-pigs.

Previously sensitized guinea-pigs may undergo marked variations in their cutaneous reactivity to neoarsphenamine.

There seemed to be an X factor, as yet unrecognized, which is essential for the production of cutaneous idiosyncrasy to neoarsphenamine in guinea-pigs.

Case Reports

SCLERODERMA CIRCUMSCRIPTUM EN COUP DE SABRE

JAMES HERBERT MITCHELL, M D, CHICAGO

The occurrence of bandlike scleroderma circumscriptum of the forehead and scalp is sufficiently rare to make the recording of two cases of some interest. The first case was presented at the April meeting of the Chicago Dermatological Society in 1927¹



Fig 1 (case 1) —Scleroderma circumscriptum en coup de sabre

The patient was a nurse, aged 31, who had had a lesion on the right of the vertex for four years. The lesion began in the midline and gradually spread laterally and posteriorly. The hair fell out and did not grow in again. At the time of the onset the patient had lost weight but had since regained it. The basal metabolic rate had remained normal.

The lesion consisted of a fine, even band of waxy, hard scleroderma about 2.5 cm in width from the hair line of the forehead half-way back to the crown. From the hair line to the right of the bridge of the nose there was a band of similar scleroderma the size of a pencil. The patient had an abscessed tooth on the upper right side which was to be extracted. After extraction of the tooth the patient left the city and has not been seen since.

¹ Mitchell, J H Scleroderma of the Scalp, Arch Dermat & Syph 17: 253 (Feb) 1928

The second case was presented at the March meeting of the same society in 1936

The patient was a boy aged 16 years. The lesion had appeared twelve years before and was not preceded by any local disturbance so far as known. There had been no pain at any time. The right nares had always been more or less closed, and the patient had difficulty in blowing the nose. There was a moderate degree of exophthalmos. The patient's mentality was good, and he had no difficulty in keeping up with his work in the first year of high school. No radiotherapy had been received. The boy was taken to a radiologist about two years after the onset of the condition, and treatment with radium was advised. However, the fee was prohibitive and none was given.



Fig 2 (case 2) —Scleroderma circumscriptum en coup de sabre

The lesion, about 11 cm in length, extended from the right supra-orbital notch upward to the right of the median line and for 3 cm beyond the hair line of the forehead into the scalp. It was 2 cm in width on the forehead, tapering to a point at the notch. The portion of the lesion on the scalp was firm and white, but the lower portion on the forehead was soft and somewhat pigmented. There was a marked depression in the portion on the forehead, and with the examining finger one obtained the impression of a loss of bone substance.

Dr Nora Brandenburg examined the patient and reported as follows: "The patient had marked nasal obstruction due to a deflected septum and a very high palatal arch. The nasal obstruction apparently was due to a deflection and dislocation of the quadrilateral cartilage of the septum. The anterior border of the cartilage was completely dislocated out of the columella and crista incisiva to the left, causing narrowing of the left ala. A large left inferior turbinate bone also helped to obstruct the left vestibule. The deflection of the septal cartilage

was so great to the right that it completely closed the right vestibule by impinging on the right inferior turbinate bone. This point of contact between the cartilage and the turbinate bone was bathed in a mucopurulent discharge. Both maxillary antrums were indistinct on transillumination. The frontal sinuses were clear. Impacted cerumen was present in the right external auditory canal. There was marked thickening of the cartilage of the left auricle with angulation, causing narrowing of the external auditory canal. Impacted cerumen was present also in the left canal. Submucous resection and removal of the impacted cerumen from the ears would improve the patient's condition."

No roentgenogram or basal metabolic test had been made. The dentition was apparently entirely normal. The boy was one of a family of four children, aged 11, 16, 19 and 20. The Wassermann reaction was negative. The mother had had no miscarriage or stillbirth.

Clinical Notes

TINEA SYCOSIS OF THE UPPER LIP

THEODORF K LAWLESS, M D,* CHICAGO

Since tinea sycosis of the upper lip alone seems to be a rare clinical entity, I wish to add the following case report to those recently recorded by Williams¹ and Davidson²

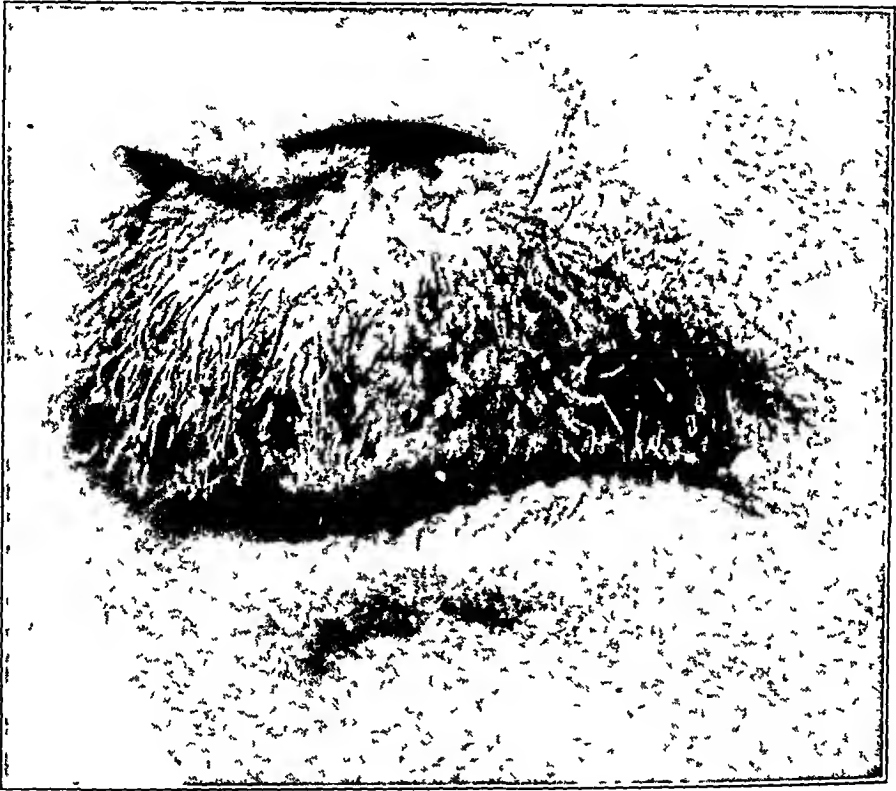


Fig 1—Tinea sycosis of the upper lip

REPORT OF A CASE

N N, aged 50, unemployed for three years, was admitted to the dermatologic clinic, suffering from a swelling of the upper lip of three weeks' duration (fig 1). In the center of the upper lip was a markedly inflammatory edematous lesion. The borders were well margined, and the surface showed many large follicular

From the Department of Dermatology and Syphilology, Northwestern University Medical School

*Elizabeth J Ward Research Fellow

1 Williams, C M Tinea Barbae Involving the Upper Lip and Accompanied by Dermatophytid, Arch Dermat & Syph 23 213 (Feb) 1931

2 Davidson, A M, and Dowding, E S Tinea Barbae of the Upper Lip, Arch Dermat & Syph 26 660 (Oct) 1932

pustules, of which some were devoid of hair and some were pustular plaques. All of these lesions were deep-seated. The hairs in the involved area were easily removed.

A 20 per cent solution of potassium hydroxide determined the classification of the invading organism as *Trichophyton endo-ectothrix*. Cultures were made on maltose agar (French maltose and peptone). The original implantation of small pieces of hair showed pure culture after ten days. The growth was characterized by a smooth, round central cupula, with radiations from it resembling many closely

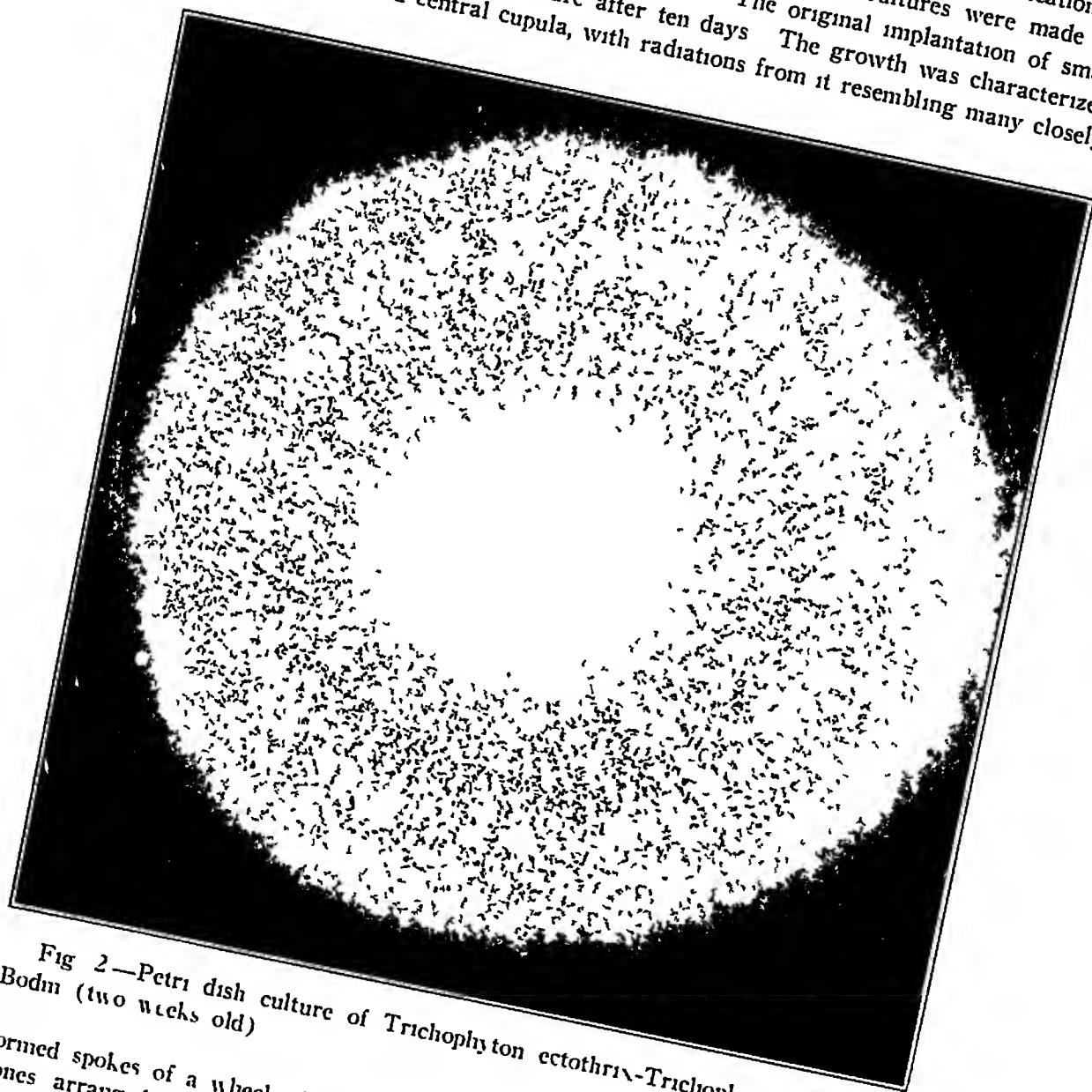


Fig 2—Petri dish culture of *Trichophyton ectothrix-Trichophyton gypsum*, Bodin (two weeks old)

formed spokes of a wheel. That part of the growth had definite thick and thin zones arranged centrifugally. The growth was coarse and pale yellow. The surface showed innumerable pearls of condensation. The outermost zone of the culture was composed of a fine, smooth lacelike whitish zone. As the culture aged the central portion was quickly covered by duvet and the color deepened (fig 2).

Microscopic examination of this culture showed the presence of pluriseptate spindles and alarospores (fig 3). These characteristics, together with the



FIG 3—Hanging-drop culture, showing aleuriospores or meristem spores and club-shaped fuseaux.

macroscopic appearance, supported the diagnosis of *Trichophyton ectothrix-Trichophyton gypseum*, Bodin. An injection of 0.1 cc of trichophytin intracutaneously gave a strongly positive reaction.

The treatment was as follows. Irregular and careless manual epilation was done by the patient. Six weekly intramuscular injections of a 1:50 dilution of trichophytin, beginning with 0.1 cc and increasing by 0.1 cc at each injection, were given, and then five injections of a 1:30 dilution, beginning with 0.4 cc and increasing by 0.1 cc at each injection. After the fourth injection had been given the lesions disappeared. More than a year afterward the patient was again seen. There had not been a recurrence of the condition.

SUMMARY

A report is given of a case of tinea infection of the upper lip alone.

The diagnosis was confirmed by means of a potassium hydroxide preparation and by culture.

Treatment with trichophytin alone was successful.

Minor Notes

A SIMPLE PRACTICAL METHOD OF ADMINISTERING ARSPHENAMINE

A B LOVEMAN, M D, LOUISVILLE, KY

The advantages of arsphenamine over the other arsenical preparations are generally known. Many syphilographers fail to take advantage of its increased efficiency because of the difficulty of preparation and administration. This paper deals merely with the technic of administration. No noteworthy deviation from the usual technic of preparation is made, except that previously prepared commercial sodium hydroxide is employed.

The following apparatus, employed by me, can be modified to suit the individual administrator. (1) a graduated rubber-stoppered bottle (from 200 to 300 cc capacity), (2) two glass tubes, one sufficiently long to reach the bottom, to act as a conductor of the fluid, and the other a relatively short one used to prevent the formation of a vacuum within the bottle, (3) one 10 to 12 inch (25 to 30 cm) section of gum rubber tubing with a glass window, (4) one glass T-shaped bivalved adapter, (5) one 5 to 10 cc eccentric tipped syringe and (6) one intravenous needle. The bivalved adapter is shown in figure 1. It is about 2 inches (5 cm) long, and one end is so ground as to fit any size of needle. To the other arm is attached the piece of rubber tubing connected with the fluid which is to be injected. The adapter is so constructed that it permits the intake of fluids only through one arm and the exit only through the other. No manipulation of valves is necessary. The instrument is light, sterilizable and inexpensive and does not clog. When one pulls back the plunger to fill the syringe, a small amount of blood will be seen to enter the tip of the valve nearest the needle. This enables one to know at all times whether or not the needle is inserted into the vein of the patient. If there is not a flow of blood, the patient may be told to "make a fist" with the tourniquet applied. If the needle is in the vein, a small amount of blood will be forced back through the tip of the valve nearest the needle. In order to fill the system at the beginning of treatment, one should hold either the gloved finger or sterile gauze over this tip of the valve when pulling back the plunger. This allows the maximum of suction to take place.

I make no claim for originality of this set-up. I merely felt that a safe and simple method could be devised for administering arsphenamine in private practice and set out to develop one. The bivalved glass adapter was the solution. Although the method has its chief advantages for the administration of single doses, it can be used also for multiple doses. If this is done, additional adapters and rubber tubing should be on hand. This method is not an attempt to replace the gravity method for clinical administration, but I feel that it is a step forward in the administration of arsphenamine in private practice. Although I have given only between fifty and seventy-five injections with this technic, there have been no undesirable reactions, and I am still employing the original bivalved adapter. It is most important, however, that the injections be given slowly, at a rate of about 5 to 10 cc per minute.

Among the advantages of such an apparatus are (1) The old tubing reaction is practically eliminated or is certainly less likely to occur, (2) there is better regulation of the rate of flow of fluid, (3) it is easier to keep the solution

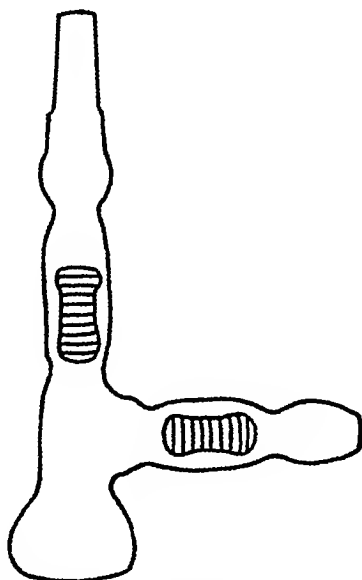


Fig 1—The adapter (actual size) The glass valves are shown by the shaded portion

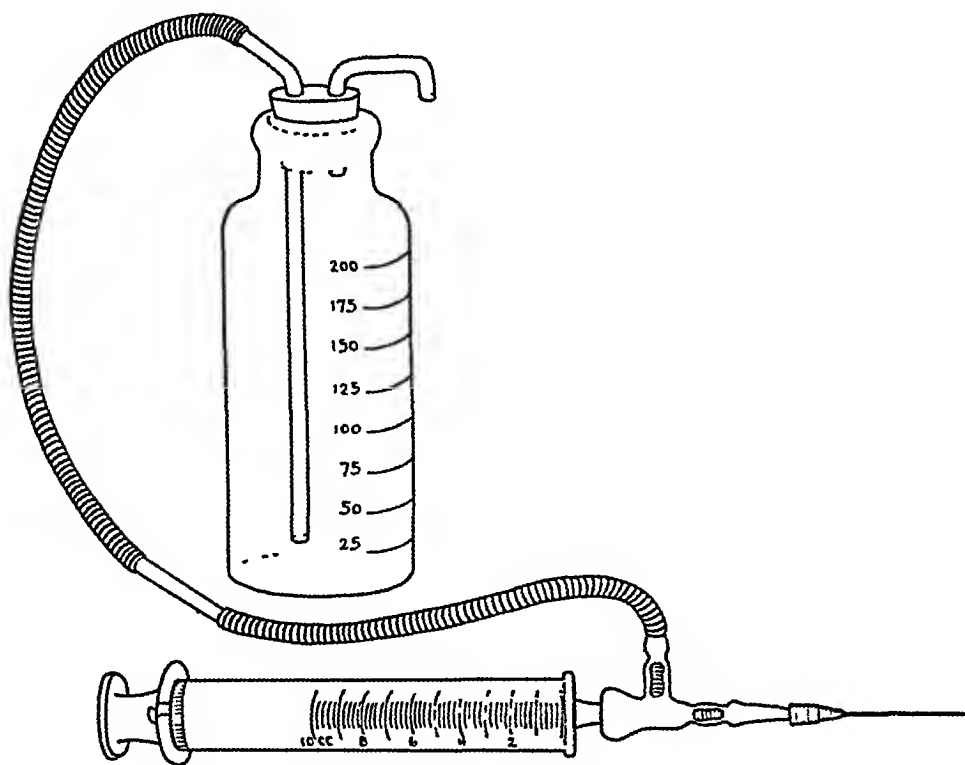


Fig 2—The complete apparatus

at the proper temperature, (4) smaller needles (even hypodermic size if necessary) may be employed (5) there is no need for elaborate apparatus, such as long tubing and large burets, etc (6) the method entails no great expense (the bivalved adapter costs \$2), and (7) it works

Correspondence

THE SO-CALLED LIBMAN-SACKS SYNDROME

To the Editor —The article by Belote and Ratner in the April 1936 issue of the ARCHIVES (vol 33, p 642) has served to call to the attention of dermatologists the occurrence of a peculiar variety of endocarditis which is separate and distinct from that of rheumatic heart disease and subacute bacterial endocarditis (Libman and Sacks) It is, however, apparent that the subject of acute lupus erythematosus has fallen into a state of obfuscation The discussions following the presentation of this paper are admirable, but the general effect is to leave the reader confused because of the differences in the point of view held by the various men It is for this reason that I beg leave to make an attempt to clarify several important issues that have arisen The implied query of Belote and Ratner of whether there is a disease peculiar to the Mount Sinai Hospital may be answered categorically in the negative It is, however, not surprising that this question has arisen, because there are publications in which the impression is left with the reader that the general disease described is new or that it has not been recognized heretofore I find myself in disagreement with this point of view for many reasons It is likely that the syndrome reported by Belote and Ratner is none other than acute lupus erythematosus, as described originally by Kaposi (1869-1872) Credit is due Libman and Sacks for a masterly report on atypical verrucous endocarditis, a morphologic and clinical conception which attracted attention to a peculiar condition and which stimulated my interest in the subject of acute lupus erythematosus in 1930 It is my belief that this type of endocarditis, when encountered post mortem in acute lupus erythematosus, is part of the disease but that it is found only in a certain percentage of the cases, estimated roughly at from 30 to 50 (Gross) It is also encountered in patients presenting atrophic lesions of lupus erythematosus However, certain qualifications must be made in order to appreciate the ramifications of this complex subject 1 It is probable that the morphologic conception of this variety of endocarditis has not yet been fully defined or the precise limits established 2 It is likely that a similar type of endocarditis may be found in several other obscure conditions, which may or may not be related to acute lupus erythematosus 3 The condition is probably often missed at postmortem examination, particularly when lesions are present on, or are confined to, the mural endocardium, and it was overlooked in many institutions for a long time, until the classic report of Libman and Sacks appeared In some cases it is probably labeled atypical rheumatic heart disease or subacute bacterial endocarditis, from which Libman and Sacks were the first to differentiate it on clinical and pathologic grounds 4 Its presence can often be suspected when there is clinical evidence of pericarditis, as the two conditions frequently occur together, however, this rule admits of many exceptions Diagnosis on the basis of valvular signs is unsatisfactory and resolves itself into a guess, which is as often wrong as right 5 When organic physical signs of endocardial origin are noted, they are usually found to be attributable to concomitant valvular deformities Whether these advanced changes are to be classified as old rheumatic cardiovalvular disease or whether atypical verrucous endocarditis can result in such alterations is still a moot point The absence

of Aschoff bodies (Libman and Gross) constitutes definite evidence against the assumption that the patients afflicted with this disorder had died as a consequence of active rheumatic heart disease

Thus, there occurs in a certain percentage of cases of acute lupus erythematosus a peculiar variety of endocarditis (valvular and mural) which can be classified as the Libman-Sacks type. The precise conception of this type of endocarditis and its variants awaits further clarification. It is my belief, also, that there is a group of cases which in the past have been correctly classified as instances of acute lupus erythematosus, and it is likely that Kaposi made a fundamental and brilliant contribution when he allied the condition in these cases to the atrophic variety of lupus erythematosus. In another place I shall bring together additional data that illustrate this relation. Regarding the tuberculous etiology of the acute variety of lupus erythematosus, which lends itself more readily to post-mortem study from this point of view, it is interesting to note that the results of the more recent autopsies and investigations are confirmatory of the conclusions found in my paper on this subject. Although the French school is still convinced of the essential part played by tuberculosis in the causation of the condition, it is of great interest that Pautrier, one of the original and warmest advocates of this hypothesis, has recently become hesitant in regard to this view.

The remainder of this letter will be concerned with the following two fundamental questions

1 Is the condition in the case recorded by Belote and Ratner a subvariety of the Osler "erythema group of diseases," and, if such is the case, what is the significance of this classification?

2 Is there evidence that the "lupus erythematosus-like" eruption of the Libman-Sacks syndrome is "erythema multiforme," representing a bacteria-free phase of a previous sepsis?

1 The conception proposed by Osler in a series of brilliant papers (1888 to 1916) is important for several reasons

(a) The conception represented a distinct advance over that of Henoch and his pupils in that eruptions other than purpura were included in this group. In more modern terms, the preponderant number of his cases may be classed as instances of "capillary toxicosis" (Frank), a term which includes the Osler-Henoch-Schonlein group.

(b) Osler was among the first to imply correctly, on clinical grounds alone, that the visceral phenomena were probably analogous to the cutaneous manifestations from a clinical and a pathologic point of view. With the exception of a single postmortem examination, the organs (kidneys) of which were shown to him by MacCallum, he recorded no other pathologic data.

(c) Osler emphasized the features of abdominal crises and other gastrointestinal symptoms manifested in twenty-five of his twenty-nine cases, and he stressed the important surgical implications.

To Osler, therefore, one owes credit for the brilliant clinical conception of a generalized disease with varied cutaneous manifestations. However, in his last casuistic report there were included four cases in which the condition was unlike that in the others reported. I am concerned only with two of them, namely, case 19 and case 26, both of which were, in all probability, instances of acute lupus erythematosus. Without going into any great detail, it must be admitted that the group of cases recorded by Osler is heterogeneous since it was the avowed purpose of Osler to seek similarities rather than dissimilarities. It seems advisable, on clinical and pathologic grounds as they are understood today, to separate these two instances with their peculiar and distinctive clinical pictures. Finally, it must

be emphasized that, as in these two cases in Osler's series, visceral crises in the sense of an acute abdominal condition necessitating surgical intervention are uncommon and do not form a distinctive part of the clinical picture that was so characteristically encountered in twenty-five of the twenty-nine cases recorded by Osler. It is my purpose to discuss elsewhere the few exceptions to this rule.

I therefore am unable to agree that the classification of the condition in the case reported by Belote and Ratner as a member of Osler's erythema group marks an advance in clinical conception.

2 The second question is divisible into three parts, each of which will be considered briefly and the details given elsewhere.

(a) The term lupus erythematosus-like implies a disease separate and distinct from the dermatologic lupus erythematosus and is, moreover, used by those who wish to deny the relation of the syndrome to that described by Kaposi or to atrophic lupus erythematosus. My observations are in disagreement with this point of view. The crux of the problem appears to rest on the contention that atrophy of the cutis is an essential requirement for the diagnosis of lupus erythematosus. Jadassohn, Brocq, Pernet and others had already stressed the point that there are cases of this disorder in which the element of atrophy is absent. My observations are in agreement with this point of view.

(b) The term erythema multiforme represents a veritable *caput mortuum* for a large number of dermatoses the classification of which is obscure. It will be shown elsewhere that there are at least four similar but distinctive varieties classified as erythema multiforme and that these may be differentiated from one another, in most instances, by careful attention to the morphologic attributes, the cutaneous clinical course and the internal medical aspects. That acute lupus erythematosus can manifest itself in the form of eruptive elements simulating "erythema multiforme" is well known, but it is my belief that such similarities, though occasionally striking, do not warrant inclusion of the conditions in a common group any more than the fact that the Henoch syndrome is occasionally diagnosed as ordinary appendicitis warrants the statement that they are related conditions. The term chronic erythema multiforme, so often used to designate acute lupus erythematosus, is, in my opinion, an unhappy expression employed by many to designate a variety of dermatoses.

(c) That acute lupus erythematosus (or the Libman-Sacks syndrome in the sense of Belote and Ratner) represents a bacteria-free phase of a previous sepsis is an attractive hypothesis, but everything about this view remains to be proved. As far as cases of acute lupus erythematosus are concerned, it may be stated that bacteriologic studies reveal the absence of known bacterial agents, the few positive results that have been obtained are susceptible of many other interpretations. It is true that the clinical picture reminds one of a severe infection or toxemia, but there is thus far no definite proof that the patients are at any time suffering from the effects of bacteremia attributable to known organisms (within the modern meaning of the term bacteremia), and the clinical picture is usually not that considered to be characteristic of ordinary "phlebitis sepsis." The demonstration of tubercle bacilli by the Lowenstein method of blood culture has been recorded, but the results published by various investigators are so discordant and the interpretation and evaluation of the positive findings so susceptible of criticism (Topley) that it must remain for the future to determine the value of the method in relation to the problem of lupus erythematosus.

HARRY KEIL, M.D., 509 Madison Avenue, New York

News and Comment

PERSONAL

Dr Edward R Maloney has been appointed visiting dermatologist and syphilologist to Bellevue Hospital, taking the place of Dr Mihran B Parounagian, who has resigned because of ill health. Dr Howard Fox has been appointed visiting dermatologist and syphilologist in charge of the combined services.

Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

SYPHILIS AND PRIMARY GLAUCOMA WALTER BECKH, *Am J Ophth* 18 1129 (Dec) 1935

A series of 288 white patients and 77 Negroes with primary glaucoma formed the basis of the study. The incidence of syphilis was lower in both groups than in a similar number of patients admitted to the medical service. In the group of white patients with glaucoma the incidence of syphilis was lower than among white patients with cataract, but in the group of Negroes the incidence of syphilis was higher among patients with glaucoma than among those with cataract. A study of the age at onset of the glaucoma in the group of white patients showed that the syphilitic patients were three years older than the nonsyphilitic patients when the glaucomatous symptoms appeared, whereas among the Negro patients no such differences existed. In 18 of the 22 patients with syphilis, the disease was latent, 2 had asymptomatic neurosyphilis, 1 had demonstrable cardiovascular syphilis and another was suspected of having it. The syphilitic patients, treated with antisyphilitic as well as miotic therapy, responded somewhat less promptly than the nonsyphilitic patients, who were treated with miotics alone.

WIEDER, Milwaukee

A GANGLIONEUROMA IN THE NECK OF A CHILD J MACFARLAND and S W SAPPINGTON, *Am J Path* 11 429, 1935

The case described is one of well characterized ganglioneuroma. In this tumor, however, nerve cells in all stages of development from neuroblasts to ganglion cells occurred, and among them was a stroma made up of Schwann cells and nerve fibers. It occurred in the neck of a little girl, and the case seems to be the twelfth of its kind to be placed on record. Three years after operative removal the patient was living, and no return of the tumor and no metastases had occurred. Appended to the article are one hundred and forty-three references to the literature.

FROM THE AUTHORS' SUMMARY [*Am J Dis Child*]

THE VIRUS OF LYMPHOGRANULOMA INGUINALE R D'AUNOY, E VON HAAM and L LICHTENSTEIN, *Am J Path* 11 737, 1935

Seven endemic strains of the virus of lymphogranuloma inguinale have been isolated and transmitted to animals. Intracerebral inoculation of infectious material produced typical meningo-encephalitis in the common marmoset whereas the rhesus monkey proved resistant to such inoculations. The virus could readily be transmitted to white mice, biweekly inoculation allowing upkeep of its maximal virulence. Emulsions of brain from infected monkeys and mice act excellently as stable and sensitive antigens for the specific diagnostic intradermal reaction of Frei. Twenty-eight per cent of infected guinea-pigs showed enlargement of the regional lymph glands with histologic lesions consistent with the disease. Experiments with sheep, chickens and frogs indicate that the virus can infect sheep, that its virulence can be preserved in the brains of chickens and that frogs cannot be infected.

THE CUTANEOUS GLOMUS AND ITS TUMOR—GLOMANGIOMA O T BAILEY, *Am J Path* 11 915, 1935

The cutaneous glomus is an arteriovenous anastomosis in the stratum reticulare of the cutis, which is homologous with the glomus coccygeum and several less important vascular structures. These have in common a specialized cell, which is

a modified smooth muscle cell with abundant nervous connections. The cutaneous glomus has an important function as an arteriovenous shunt in maintaining the body temperature and perhaps the blood pressure. From the cutaneous glomus, a tumor may arise which forms a subgroup of the hemangioma. The term "glomangioma" is suggested for it to indicate its derivation and character. Glomangioma appears as a small bluish nodule on an extremity or an adjacent portion of the shoulder girdle. Very frequently it is located in the nail bed. Microscopically the tumor is composed of cells identical with those in the walls of the normal cutaneous glomus and its homologue. Nerve trunks are numerous in the connective tissue about the tumor, and nerve filaments pass among the glomus cells in large numbers. Occasionally elongate smooth muscle cells are seen either in solid masses or adjacent to vascular lumens. The glomangioma represents the overgrowth of the entire arteriovenous anastomosis, and the cells show a twofold differentiation. First, the elongate smooth muscle cells lose all myofibrils, while the reticulum investing them becomes much coarser and stains intensely with collagen stains. Second, the periglomic nerves grow into the tumor, and their terminal filaments end about the differentiating smooth muscle cells with the interposition of nerve endings. These two processes result in the formation of the glomus cells and are apparently interdependent. The tumor is associated clinically with severe radiating pain of neuralgic type. In character and distribution this has many similarities to the response of the normal glomus to much greater stimuli of the same character. Glomangiomas thus represent functionally as well as morphologically organoid overgrowths. Glomangiomas do not become malignant. Local excision gives complete and permanent relief from symptoms.

FROM THE AUTHOR'S SUMMARY [ARCH PATH]

RADIUM DOSAGE AND TECHNIQUE IN BENIGN LESIONS OF THE SKIN. HOWARD MORROW and LAWRENCE R. TAUSSIG, *Am J Roentgenol* 32:735 (Dec) 1934

The limitations of the use of radium due to the danger of late sequelae, such as telangiectasia, atrophy, keratosis and malignant growth, are outlined, and a method of guarding against such sequelae is given. Roentgen therapy has proved superior to radium in the treatment of many diseases, such as psoriasis, lichen planus, eczema, etc. The authors outline the treatment and give the dosages of radium for the following conditions: congenital anomalies, such as vascular and fleshy nevi, and acquired conditions, such as keloid, verruca, synovial cyst and epulis.

SQUIRES, Chicago [AM J DIS CHILD]

CUTANEOUS TUBERCULOSIS AND GENERAL MEDICAL DIAGNOSIS. FRANCIS E. SENEAR, *Ann Int Med* 8:1274 (April) 1935

In this article, which deals with diseases of the skin bearing a relationship to tuberculosis, Senear states that erythema nodosum occurring in children is frequently of tuberculous origin. It tends to occur early in the course of tuberculous disease and necessitates prolonged convalescence and careful observation for at least six months.

Erythema nodosum of tuberculous origin is apt to occur in unusual locations and exhibits a greater tendency to localize on the posterior aspect of the legs. The nodules are smaller and tend to be less numerous and acute, and the process as a whole is less active than when the disorder is due to other causes.

It is also suggested that erythema multiforme may be of tuberculous origin in a small proportion of cases.

READING, Galveston, Texas [AM J DIS CHILD]

THE ANORECTAL PHASE OF LYMPHOGRANULOMA INGUINALE. A. W. MARTIN MARINO, *Ann Surg* 102:1086 (Dec) 1935

Three cases of lymphogranuloma inguinale, two occurring in white women and the third in a Negress, are described. In one of these patients, a white woman, the process had caused the entire rectum and the sigmoid and descending portions

of the colon to be stenosed owing to infiltration of all the coats. In the three patients there were, respectively, rectal stricture with perianal fistula, rectal stricture with perianal elephantiasis and rectal stricture with elephantiasis complicated by perianal fistula. The three patients received several courses of antimony and potassium tartrate intravenously without appreciable benefit.

WIEDER, Milwaukee

RELATIONSHIP OF PELLAGROUS DERMATITIS TO SUNLIGHT T D SPIES, Arch Int Med 56:920 (Nov) 1935

In this study pellagrins receiving a diet of 2,900 calories but low in pellagra-preventive substances were exposed to radiation from a quartz mercury vapor arc lamp, areas of skin that appeared normal and some pellagrous lesions being irradiated.

The effect of dermatitis, pigmentation and desquamation was produced on the normal appearing skin, but the reaction could not be diagnosed as pellagrous. The pellagrous lesions became more deeply pigmented but the irradiation did not prevent their healing.

Normal persons and pellagrins were exposed in an identical manner to sunlight, but the resulting reaction showed no difference in intensity or character.

Four patients who had been cured of pellagra were given a deficient diet and kept from exposure to sunlight. Within six weeks the characteristic dermal and other changes developed.

Spies considers that pellagra should be regarded as a systemic disease which is the real cause of pellagrous dermatitis, but he believes that under certain conditions sunlight may act as the precipitating irritant in the production of the cutaneous lesions.

DIFFERENTIAL DIAGNOSIS OF RUBELLA USE OF THE SCHILLING DIFFERENTIAL LEUKOCYTE COUNT C M MACBRYDE and C M CHARLES, Arch Int Med 56:935 (Nov) 1935

Serial differential blood counts by the Schilling method were made by MacBryde and Charles in thirty cases of rubella. The authors believe that these counts differed significantly from the counts obtained in other conditions—chiefly measles, scarlatina and toxic rashes—which might be confused with rubella.

JAMIESON, Detroit

AN ATYPICAL FAMILIAL ENDOCRINOPATHY IN MALES WITH A SYNDROME OF OTHER DEFECTS WILLIAM ANTHONY REILLY, Endocrinology 19:639 (Nov-Dec) 1935

Reilly reports three cases of a syndrome first described by Hunter in 1917. It is familial, occurs only in male children and is characterized by optic neuritis, a typical physical appearance due to similar facies, changes in the bones and joints, hepatosplenomegaly and coarseness, dryness and thickness of the hair.

In the author's first case the skin was thick, coarse and freckled and the tongue was enlarged and rough. At autopsy areas of degeneration and necrosis were observed in the anterior lobe of the pituitary body. There was also mild hyperplasia of the thyroid gland.

In the second case there was a similar clinical picture, but a biopsy of the skin showed only a mild chronic nonspecific dermatitis. Reilly does not mention results of stains for mucin.

In the third case the skin and hair were dry and coarse, and there was increased growth of hair on the face, arms and eyebrows.

Reilly states that although the facies, tongue, hair, texture and appearance of the skin suggested hypothyroidism and other signs suggested hypopituitarism, many features of the syndrome could not be explained merely on a basis of endocrinopathy.

LYNCH, St Paul

THE INFLUENCE OF LATENT SYPHILITIC INFECTION ON THE REACTION OF THE RABBIT TO THE BROWN-PEARCE TUMOR P D ROSAHN, J Exper Med 62: 213 (Aug) 1935

As a result of this experimental work Rosahn found a lower mortality rate in the combined group (fifty rabbits of five breeds) than in the control group of normal nonsyphilitic rabbits. This was also true for each individual breed.

Relative resistance of the different breeds to the Brown-Pearce tumor was not altered by the latent syphilitic infection.

There was also found a high correlation between the resistance of the breed to infection with *Spirochaeta pallida* and the resistance to the Brown-Pearce tumor.

CUTANEOUS REACTIVITY OF IMMUNE AND HYPERSENSITIVE RABBITS TO INTRADERMAL INJECTIONS OF HOMOLOGOUS INDIFFERENT STREPTOCOCCUS AND ITS FRACTIONS C McEWEN and H F SWIFT, J Exper Med 62: 573 (Oct) 1935

McEwen and Swift inoculated rabbits intradermally with a soluble streptococcus protein after having immunized them intravenously with the same protein. The result was an immediate anaphylactic type of dermal response. However, in the rabbits immunized by intracutaneous inoculation of the intact organism and subsequently tested in the same manner by intradermal inoculation a delayed type of response was elicited.

JAMIESON, Detroit

INFANTILE ECZEMA W O COLBURN, Nebraska M J 20: 21 (Jan) 1935

Cutaneous tests are not recommended for the determination of the offending protein in infantile eczema. The results are unreliable in children less than 6 months of age. Desensitization by subcutaneous use of the mother's milk, which is boiled in a water bath for three minutes is recommended. The doses start with 1 minim (0.06 cc) and are increased 1 minim every other day until 4 minims (0.24 cc) is given, they are then given twice weekly and are increased 1 minim for each dose until from ten to fifteen doses have been given, depending on the results.

HAMILTON, Omaha [AM J DIS CHILD]

CHRONIC ATROPHIC DERMATITIS OF THE VULVA F L ADAIR and M E DAVIS, Surg, Gynec & Obst 61: 433, 1935

The descriptive term employed here is preferable to any of the many names hitherto proposed because it indicates the nature of the entire process rather than emphasizes only certain phases of the condition. Among patients with gynecologic disorders seen by the writers the incidence of the lesion at one stage or another was 0.24 per cent. It is a progressive disease and, unless vulvectomy is performed, leads to carcinoma in more than half of the cases. The three stages of the lesion are excellently depicted in colored plates.

HUNTER, Portland, Ore [ARCH PATH]

STUDIES IN CHEMOTHERAPY XII THE DIFFUSIBILITY OF THE AROMATIC ARSENICALS INTO ERYTHROCYTES AND THE ACTION OF THE LATTER ON THE PENTAVALENT ARSENICALS E M LOURIE, F MURGATROYD and W YORKE, Ann Trop Med 29: 265 (July) 1935

Lourie, Murgatroyd and Yorke found that when red blood cells were suspended in a solution of tryparsamide in Ringer's solution with glucose a certain amount of the drug rapidly passed into the red cells. The laked red cells, after separation from the drug solution, were powerfully trypanocidal.

If the red cells were suspended for twenty-four hours in the solution containing tryparsamide the laked blood cells were found to contain approximately twice as much tryparsamide as after a fifteen minute exposure. However, if these cells were treated by washing, less of the drug could be recovered than after the shorter exposure, this suggested that some of the drug is more firmly bound to the substance of the red cells during the longer exposure.

JAMIESON, Detroit

CUTANEOUS MYIASIS IN INFANTS N SILVERTHORNE and A BROWN, Arch Dis Childhood 9 339 (Dec) 1934

Three cases of cutaneous myiasis produced by larvae of *Wohlfahrtia vigil* (Walker) in infants are reported. The larvae are discharged on the surface of the patient's skin by the gravid fly. The larvae quickly migrate to areas where there are folds and burrow into the subcutaneous tissue, producing an inflammatory reaction. The lesions disappear after the larvae are removed, either by forceps or by squeezing. In the three cases reported, larvae removed from the lesions of the skin were reared to adult flies. The lesions occurred in healthy infants sleeping outdoors during June.

PAPULAR URTICARIA (LICHEN URTICATUS) B C TATE, Arch Dis Childhood 10 27 (Feb) 1935

A thorough investigation, mainly of the etiology, of this cutaneous disease is reported, with the following conclusions:

Papular urticaria is a definite and distinct syndrome, distinguishable from urticaria and from Hebra's prurigo. It is a manifestation of allergy. It is essentially a disorder of the first four years of life. It is aggravated by heat and by a diet containing too much carbohydrate. Digestive disorders, teething and mild febrile disturbances probably predispose to papular urticaria, but such conditions are of minor importance in the etiology. Rickets plays no part. There is no satisfactory evidence of any underlying diathesis. The exciting agent is not a food but something connected with the home environment of the patient, the precise nature of which remains obscure. The agent is not bedding or clothes, but it can be carried on these articles. It is not vermin or an antigen derived from human beings or domestic animals. Sensitivity to house dust has not been definitely excluded.

KELLY, Milwaukee [AM J DIS CHILD]

PRESENCE OF HEMOLYTIC AND OTHER STREPTOCOCCI ON HUMAN SKIN L COLEBROOK, W R MAXTED and A M JOHNS, J Path & Bact 41 521, 1935

Hemolytic streptococci of the kind usually associated with human puerperal infections (Lancefield's group A) were not found on the perineal and perianal skin of 160 women attending an antenatal department, and the risk of such streptococci being conveyed to the genital tract from the feces is considered to be remote. Group A hemolytic streptococci were isolated from the hands of 7 of 181 normal persons (3.8 per cent). It seems probable that they were derived from the respiratory tract. Treatment of the mother's hands during labor by an antiseptic is advocated. Nonhemolytic types of streptococci (chiefly *Streptococcus viridans*) were found on nearly all the hands investigated but not on the skin of the interscapular region.

FROM THE AUTHORS' SUMMARY [ARCH PATH]

THE ULCER SYNDROME IN TROPICAL AFRICA A A F BROWN, J Trop Med 38 157 (July 1) 1935

Brown classifies ulcers into groups A, B and C. Ulcers of group A are about the same all over the world, they are due to trauma, scabies, yaws, etc. Ulcers of group B are typical phagedenic ulcers, frequently arising from a vesicle. Those of group C are clinically identical with those of group B, but they are due to trauma and become phagedenic later on.

He analyzes the observations on ulcers during a five year period and expresses the belief that a strong correlation exists between *Bacillus fusiformis* and *Spiro-nema* and the phagedenic type of ulcer. In the laboratory it was impossible to obtain a pure culture of *B. fusiformis* alone.

Clinically ulcers were phagedenic and nonphagedenic. Forty-six and one-tenth per cent of the ulcers in Brown's series failed to reveal *B. fusiformis*.

In a series of 423 males examined bacteriologically 53.9 per cent showed *B. fusiformis* and/or *Spirochaeta Schaudinni*, and in 89 per cent of these the ulcers were phagedenic. The presence of these organisms in a nonphagedenic ulcer indicated a change in character to the phagedenic form. (The article is to be continued.)

THE ULCER SYNDROME IN TROPICAL AFRICA A. A. F. BROWN, *J. Trop. Med.* 38:170 (July 15) 1935

In this instalment the writer discusses several questions regarding the pathogenicity of *Bacillus fusiformis* and *Spironema*. It is difficult to determine whether the phagedenic ulcers in question form a suitable medium for the organisms to develop or whether the organisms themselves produce the change from the traumatic to the phagedenic type of ulcer. Lesions of the mucous membranes due to Vincent's bacillus usually responded well to arsenic therapy while the tropical phagedenic ulcers did not. The vesicles which usually preceded the ulcers did not contain *B. fusiformis*. Inoculations of animals likewise gave negative results. Phagedenic ulcers which did not contain *B. fusiformis* were of a different type.

Brown suggests that *B. fusiformis* and *Spironema* may be the cause of phagedenic ulcer but that it is difficult to prove this point, as pure cultures of the organisms have not been obtained.

Ulcers were found slightly less often in female patients. Dietary changes were believed to be partially accountable for variations in the incidence according to tribes. Ulcers showed no improvement under treatment with arsenic, bismuth or mercury unless they were definitely of the syphilitic or jaws type.

The treatment of patients with ulcers was complicated in many instances by the presence of endoparasites, malarial organisms, hookworms, etc. (The article is to be continued.)

THE ULCER SYNDROME IN TROPICAL AFRICA A. A. F. BROWN, *J. Trop. Med.* 38:187 (Aug. 1) 1935

Treatment of ulcers consists of scraping, if necessary, of ordinary local treatment and of a standard hospital diet. If satisfactory progress does not follow in two or three weeks, calcium chloride is given intravenously in doses of 15 grains (0.97 Gm.) in 10 cc. of distilled water once or twice daily. If results are still unsatisfactory after ten days, parathyroid extract is given orally. The average duration of treatment is about six weeks.

The results of this treatment in the series of cases observed by the author indicate that a definite benefit was derived from the intravenous administration of calcium chloride. Approximately 30 per cent of the patients with phagedenic ulcers had a low calcium level. The level for phosphorus varied from a low value of 18 mg. to a high value of 112 mg. per hundred cubic centimeters of blood serum. Ulcers were not commonly found in members of tribes who consumed flesh, beans and ground nuts. It appears from this that the diet is largely responsible for the development of these ulcers.

JAMIESON, Detroit

STILL'S DISEASE WITH ERYTHEMA MULTIFORME DONALD PATERSON, *Proc. Roy. Soc. Med.* 28:157 (Dec.) 1934

A case of this condition in a boy aged 6½ years is reported. The history, the results of physical and roentgen examination and the treatment are given. The dermatologist reported that the cutaneous lesions were those of erythema multiforme, probably evidence of a former streptococcal infection.

WILLIAMSON, New Orleans [*Am. J. Dis. Child.*]

CALCINOSIS W D W BROOKS, *Quart J Med* 3 293 (July) 1934

The literature concerning calcinosis is reviewed Brooks then presents the results of his own experimental study concerning the calcium and phosphorus balance in a case of calcinosis in a girl aged 15 and also in a case of scleroderma in a woman aged 41 In the girl, pathologically high levels of serum calcium, plasma inorganic phosphate and plasma phosphatase were maintained over a long period, whereas these values were normal in the patient with scleroderma The calcium metabolism in the girl was restored to approximate balance by the administration of di-sodium hydrogen phosphate The author suggests that in calcinosis a local tissue change, not yet clearly understood, results in localized damage to fibrous tissue and that when calcification occurs in these areas an abnormality of calcium and phosphorus metabolism may also occur Brooks expresses the belief that the type of lesion in scleroderma does not necessarily produce abnormal changes of the calcium and phosphorus metabolism

BRADFORD, Rochester, N Y [*AM J Dis Child*]

OBSERVATIONS ON SYPHILIS OF THE PLACENTA M BRINDEAU and Y MANOUELIAN, *Bull Soc de pediatrie de Paris* 31 441 (Nov) 1933

The placenta of a 20 year old woman, delivered of a syphilitic infant, had the gross appearance of syphilitic involvement It was studied histologically by a silver impregnation method for the identification of *Spirochaeta pallida* The striking observation was made that the organisms were few in the placental tissue and in the blood but that in the walls of the tiny venules they were unusually plentiful, forming interlacing networks in places While some of the spirochetes were typical in morphologic characteristics, many showed various stages of change, assuming ringlet and crown shapes and losing the appearance of spirals The organisms were chiefly seen in phagocytic cells Spirochetes were also noted in the cutaneous lesions of the infant Sections of the umbilical cord showed many organisms in Wharton's jelly, and although few could be seen in the blood which filled the vein, they occurred for the most part within phagocytes

A CASE OF CYTOSTEATONECROSIS IN A NEW-BORN INFANT L BABONNEIX and DIRIART, *Bull Soc de pediatrie de Paris* 32 519 (Nov) 1934

An infant, 3 weeks old, presented marked induration of the skin over the entire back, which was violet-colored The skin was ligneous in consistency and could not be creased or raised from the deeper tissue This condition did not seem to disturb the infant, as he thrived well There was a history of trauma immediately after birth, as the obstetrician spanked him repeatedly on the back over a period of twenty minutes on account of marked asphyxia It took about a month for the skin to assume its normal characteristics The abnormal condition is due to necrosis of the subcutaneous adipose tissue

VARIOUS CASES OF ACRODYNIA AND THE TREATMENT P DUHEM and ERNEST HUANT, *Bull Soc de pediatrie de Paris* 32 527 (Nov) 1934

Six cases of acrodynia in children, ranging in age from 1 to 14 years, are described Cases of hypotonicity for which no definite cause can be found should suggest the possibility of acrodynia The first improvement which generally takes place is to be observed in the tone and disposition, this occurs long before any marked amelioration of the trophic disturbances becomes evident Investigation of the neurovegetative responses, such as the oculocardiac reflex and the cardiac acceleration, after the subcutaneous injection of a solution of epinephrine is advised, both as an aid to diagnosis and a guide in physical therapy It is believed that the most probable etiologic factor in this disease is neuro-endocrine

PRIMARY TUBERCULOUS CUTANEOUS INOCULATION AND REGIONAL ADENITIS
TREATED SURGICALLY M COFFIN, Bull Soc de pédiat de Paris **32**:535 (Nov)
1934

In a girl, 7 years old, inguinal adenitis developed after a wound on the knee, which became infected and left a violet paper-like scar. A number of inguinal glands were originally involved, but the condition subsided in all except one, in which it progressed until the tissue broke down. The glands were excised, as well as the area of unhealthy skin. Histologically tubercles were observed in the glands, and bacilli were demonstrated in them. The skin showed typical epithelioid and giant cells with involvement of a sweat gland. The child had been in contact with the father, who had tuberculosis. The reaction to the tuberculin test was positive. It is considered that in this case there was a primary tuberculous lesion of the skin, the bacilli having entered by way of a wound, and that the inguinal glands became involved by extension up the leg of bacilli through the lymphatic channels. Primary tuberculosis of the skin is serious in infants, who may succumb to the infection, but in older children the prognosis is much better. When the skin is secondarily involved by tubercle bacilli which originate in other foci in the body, the lymph glands in the region of the infected skin do not usually cascade.

BENJAMIN, Montreal, Canada [AM J DIS CHILD]

FINDING OF HEMISPORA STELLATE IN RINGWORM OF THE SCALP M PAVIA, Riv
di clin pediat **33**:144 (Feb) 1935

In cultures of material taken from the lesions of ringworm of the scalp in a girl aged 7 years, the author was able to identify *Hemispora stellata* Vuillemin in pure culture, later cultures yielded *Achorion Schoenleini*. It is unusual to find *Hemispora stellata* as the etiologic agent in such lesions of the scalp.

GERSON-HERRMANNSDORFER-SAUERBRUCH DIET IN THE TREATMENT OF CHILDHOOD
TUBERCULOSIS A GOLIN and R DEMENIGHINI, Riv di clin pediat **33** 257
(March) 1935

Thirty children between the ages of 3 and 9 years, having various types of tuberculosis, were given a diet patterned after those of Gerson, Herrmannsdorfer and Sauerbruch. The diet is definitely low in sodium chloride and high in vegetables and fruits. A sample diet for a 6 year old child weighing 43 pounds (19.5 Kg) contained the following foods:

Milk, 500 Gm, meat, 80 Gm, vegetable purées, 100 Gm, raw or steamed greens, 100 Gm, cooked fruit, 100 Gm, raw fruit, 100 Gm, macaroni, 20 Gm, bread, salt-free, 40 Gm, butter, 20 Gm, cod liver oil, 40 Gm, and olive oil, 20 Gm.

The values of the diet were as follows: protein, 26 Gm, fat, 6 Gm, and carbohydrate, 74 Gm, per kilogram of body weight.

Sixteen of the thirty children did excellently, and nine others, fairly well, when they were fed the diet, it led not only to improved nutrition but to clinical improvement. The other five children did not do well clinically, although several showed a gain in weight and an increase in the hemoglobin concentration.

HIGGINS, Boston [AM J DIS CHILD]

HEMANGIOMAS AND LYMPHANGIOMAS RESULTS OF TREATMENT G GERLACH,
Beitr z klin Chir **159**:129, 1934

Gerlach studied all the cases observed by him between 1918 and 1933 in order to learn what method of treatment was preferable not only from the standpoint of elimination of the condition but also from that of the cosmetic results.

Eighty-four patients were treated, and fifty-one were followed up. Included among these were seventy-one patients with hemangioma, twelve with lymphangioma and one with a combination of both conditions. The hemangiomas were

treated as follows Thirty-four were excised, twenty-nine were treated with radium, two were needled with magnesium, two were punctured, two were treated with injections of alcohol and with radium and one was excised and treated with radium Treatment of the lymphangiomas was as follows Seven were excised, two were treated with radium, one was needled with magnesium and two were not treated The lesion which was a combination of hemangioma and lymphangioma was excised

Total extirpation left a small scar which faded in late years Bad results were seldom seen Treatment with radium gave good results, but from the cosmetic standpoint the results were not as good as those following surgical intervention—scars were more prominent Pigmentation around the periphery was more obvious in the patients treated with radium In several cases in which the involvement was severe good results were also obtained by needling with magnesium

RUBIN, Boston [AM J Dis Child]

THE PROPHYLACTIC EFFECT OF A SOLUBLE PREPARATION OF ARSPHENAMINE IN EXPERIMENTS WITH ANIMALS RICHARD WAGNER, *Dermat Wchnschr* 99 1609 (Dec 15) 1934

The prophylactic activity of 3, 4' di-acetyl amino-4-hydroxyarsenobenzene-2-sodium glycocholate suitable for intramuscular injection was tested on a series of rabbits The Nicholas strain of *Spirochaeta pallida* was used, and the inoculations were made by scarification of the scrotum. The manufacturers stated that the therapeutic dose of the preparation for rabbits was from 5 to 10 mg per kilogram Doses of 2.5, 5 and 10 mg per kilogram given two hours before or two hours after inoculations did not prevent the formation of the chancre It required a dose of 20 mg per kilogram to prevent development of the chancre

TREATMENT OF LUPUS ERYTHEMATOSUS WITH ESTERS OF CHAULMOOGRA AND HYDROCARPUS OIL SVEND LOMHOLT, *Dermat Wchnschr* 101 817 (July 6) 1935

Lomholt reports the results of treatment of thirty-one patients with lupus erythematosus with esters of chaulmoogra and hydnocarpus oil A brief report of cases and a number of photographs made before and after treatment are given The drug was given either intravenously in doses of from 1 to 2 cc in 9 cc of an 8 per cent solution of alcohol or intramuscularly in doses of from 1 to 2 cc with a proprietary brand of ethyl aminobenzoate either daily or two or three times a week In general Lomholt prefers the intravenous route, though the results were apparently the same Intravenous injections frequently caused brief periods of headache or shortness of breath and occasionally a rise in temperature An average of twenty injections were given each patient Of the group of patients forming the basis of this study, eleven were cured, twelve much improved, seven somewhat improved and one unimproved Finsen light was also used in some instances

THE HISTOGENESIS OF NEVUS SYRINGOCYSTADENOMATOSUS PAPILLIFERUS J DORFFEL, *Dermat Wchnschr* 101 855 (July 13) 1935

A 30 year old woman presented a warty growth in the right parietal region which had been present for at least ten years and had increased slowly in size Clinically it was a superficial epithelioma or a nevus of a sebaceous sudoriferous gland Histologic examination showed a sweat gland-like epithelial hyperplasia appearing to arise from the basal layer of the epidermis Some areas were papillary, others presented the picture of an intra-epidermal epithelioma Plasma cells were abundant in the infiltrate, and there were also numerous mast cells Dorffel is of the opinion that these observations bear out his theory of the pluripotency of epithelial cells

A SIMPLIFIED STAINING METHOD FOR DEMONSTRATING FUNGI IN SCALES AND HAIR J ALKIEWICZ and W GORNY, *Dermat Wehnschr* **101**:1034 (Aug 24) 1935

The authors found the following method satisfactory in staining fungi in scales and hair. The material is fixed and fastened to the slide by heating a few moments over a flame in a solution consisting of ten parts of a dilute solution of formaldehyde (4:10) and a hundred parts of alcohol. It is then stained in one part of cresyl violet (Grubler) and a hundred parts of 0.9 per cent solution of sodium chloride for about five seconds while being warmed gently. The preparation is then dried carefully with filter paper and mounted in oil of cloves.

TAUSSIG, San Francisco

THE DEMONSTRATION OF THALLIUM IN THE TISSUES J SCHNELLER, *Deutsche Ztschr f d ges gerichtl Med* **25** 222, 1935

Thallium was demonstrated spectroscopically in the urine and stool of a woman three and one-half months after she had ingested 0.37 Gm of the poison. It could not be detected by ordinary means. This slow excretion was confirmed in dogs and guinea-pigs poisoned with thallium. Tests showed its presence in the bones long after all traces of the metal had disappeared from other organs.

RUKSTINAT, Chicago [ARCH PATH]

TREATMENT OF NINETY-SIX PATIENTS WITH NEUROSYPHILIS BY ACTIVE IMMUNIZATION WITH NONPATHOGENIC CULTURES OF SPIROCHÆTA PALLIDA L BENEDEK, *Monatschr f Psychiat u Neurol* **88**:1 (Feb) 1934

Benedek treated ninety-six patients suffering from neurosyphilis with injections of Hilgermann's cultures of living but avirulent spirochetes. There were fifty-six patients with dementia paralytica and thirty-three with tabes. The group included elderly persons who were in poor physical condition. There was no evidence to suggest that the transfer of the avirulent strain of spirochetes to the human organism could activate the spirochetes and lead to a generalized or localized superinfection. However, focal nervous symptoms were sometimes increased temporarily. Thus, all but six of the patients with tabes showed an increase of such symptoms as lightning pains, gastric crises and paresthesia during the course of treatment. As a rule, a slight to moderate rise of temperature and moderate leukocytosis occurred. Local cutaneous or connective tissue reactions were noted in eleven patients after repeated injections of the vaccine. The formation of abscesses was observed in three patients. This was probably due to contamination of the cultures with other bacteria. Seventy-five patients had previously received some form of treatment, but only eight had shown improvement. This included two patients who had complete remissions. In sixty-nine cases the cultures of spirochetes were given in conjunction with other types of therapy. The latter consisted of one course of treatment with antisyphilitic drugs in thirty-one of these cases. Fifty-five patients showed improvement during or shortly after the administration of the vaccine, twenty-four patients showed no change, and ten became worse. One patient died during treatment, but necropsy disclosed a neurinoma of the cerebellopontile angle as the cause of death. It was possible to follow seventy-five patients for approximately from two to three years. Complete remission had occurred in thirteen, considerable improvement in twelve and slight or moderate improvement in fifteen. Sixteen members of the group had died. Better results were noted in the group with tabes than in that with dementia paralytica, 54.5 per cent of the patients in the former and 25 per cent of those in the latter group showing improvement.

The serologic reactions were studied in fifty-one cases. The Wassermann reaction of the blood became negative in four cases and that of the spinal fluid in seven cases. The colloidal gold reaction showed improvement in 49 per cent of the group, and the cell counts were diminished in 52.9 per cent. It was not

possible to determine whether there was any correlation between clinical and serologic changes, owing to the fact that the lumbar punctures were performed without regard to the clinical condition of the patients. A scrutiny of the results obtained in patients treated solely with injection of spirochetes leads Benedek to conclude that vaccine therapy is as efficacious as other forms of treatment. The results are favorable enough to suggest that with further development of the method still greater success in treatment may be obtained.

ROTHSCHILD, Foxborough, Mass [ARCH NEUROL & PSYCHIAT]

CONGENITAL ICHTHYOSIS W COURTIN, Ztschr f Kinderh 55 384 (Sept) 1933

Courtin reports the case of an infant born 4 weeks prematurely, with no family history of disease of the skin, who from the first day of life showed cornification of the skin. The picture was that of the congenital ichthyosiform erythroderma described by Brocq. The author could find no etiologic factor for the disease. He excluded syphilis.

LEVINSON, Chicago [AM J DIS CHILD]

ANIMAL EXPERIMENTATION AND THE VIRUS OF LYMPHOGRANULOMA INGUINALE
I TOYAMA, M HASEGAWA and T ICHIKAWA, Jap J Dermat & Urol
37 351 (March), 38 21 (Aug) 1935

The authors report the results of experiments with the virus of lymphogranuloma inguinale on monkeys and guinea-pigs (first communication) and on squirrels, *Eutamias orientalis* (second communication).

The material used was the pus or the macerated material from glands of patients with clinically proved lymphogranuloma inguinale who showed positive reaction to the Frei test and negative reactions to the Dmelcos, Ito and Wassermann tests. Only material which was proved to be culturally nonbacterial was employed. This material was injected intracerebrally into the monkeys and squirrels and subcutaneously, intraglandularly and intratesticularly into the guinea-pigs. The monkeys and the squirrels proved adapted to experimentation with the virus of the disease, emulsions of the brain and liver of these animals could be reinoculated into other monkeys or squirrels indiscriminately, the virus could be passed through as many as six squirrels and nine monkeys and could be used for testing the Frei reaction on other patients known to have lymphogranuloma inguinale. Even brain or liver of animals in which clinical symptoms (various pareses or paralyses of the extremities) failed to develop after inoculation furnished a potent antigen.

By means of these experiments the authors proved that the clinical entity known as inflammatory stricture of the rectum is a result of lymphogranuloma inguinale.

BRENNAN, Chicago

CONGENITAL NONSYPHILITIC PEMPHIGUS A REVIEW WITH THE DESCRIPTION OF
A NEW DISEASE (EPIDERMOLYSIS BULLOSA HEREDITARIA LETALIS) G HERLITZ,
Acta pædiat 17 315, 1935

In the differential diagnosis of bullous eruptions in the new-born infant congenital syphilis, the congenital form of pemphigus neonatorum contagiosus and epidermolysis bullosa hereditaria should be considered. Rarely, other possibilities must be considered, such as congenital variola or varicella, dermatitis herpetiformis and arsenical dermatitis. Examples of all these have been reported.

A review of the literature reveals the following facts concerning pemphigus neonatorum contagiosus. Although it is an infectious disease, it may be present at birth. The organism most commonly found in the lesions is the staphylococcus, although the streptococcus has been incriminated occasionally. The mode of infection is uncertain. The prognosis is usually good. The clinical features of both the simple and the dystrophic forms of epidermolysis bullosa hereditaria are too well known to require extensive description.

In the children's clinic of the university of Upsala, Sweden, within the last ten years eight cases of a peculiar congenital pemphigus have been encountered, the nosographic features of which are not identical with those of any of the foregoing entities. The disease is familial. The eight patients came from three families residing in different parts of the province of Upland, Sweden. All the patients were infants, both sexes were represented. At birth each patient exhibited either more or less widely distributed epidermal defects and bullous lesions or severe trophic disturbances of the nails of the fingers and toes. Usually all three types of lesions were present in the same patient. In six of the cases there was a slight tendency toward healing, in two cases atrophy of the bones and soft parts of the toes ensued. In two instances unidentified cocci were isolated from the bullae rather long after the latter had appeared. The patients usually remained afebrile. The disease was uniformly fatal within a few days or a few weeks after birth. Autopsy was performed in six cases but failed to provide significant information concerning the etiology or the pathogenesis of the condition. In one of the families the father and mother were cousins, in another the maternal grandparents were also cousins. Careful genealogic investigation of the families back to the beginning of the seventeenth century failed to unearth relevant data.

Although in these cases the condition presented several points of resemblance to epidermolysis bullosa hereditaria, it is justifiable to regard it as representing a separate entity because of the nature of the congenital epidermal defects, the atrophy of the skeleton, the fact that bullae could not be produced by means of friction and the uniformly fatal outcome. A total of fourteen cases of similar conditions have been described at different times and under different names since 1922 (Mautner, Kuse, Jenny, Heinrichsbauer). It is proposed to assemble these cases with those reported by Herlitz and to designate the condition as epidermolysis bullosa hereditaria letalis.

A copious bibliography is appended.

McCUNE, New York [AM J DIS CHILD]

Society Transactions

SAN FRANCISCO DERMATOLOGICAL ASSOCIATION

JOHN M GRAVES, M D, *Secretary*

Sept 27, 1935

L R TAUSSIG, M D, *President*

LUPUS ERYTHEMATOSUS SHOWING FEATURES OF SARCOID, RESISTANT TO GOLD SODIUM THIOSULFATE BUT RESPONDING TO BISMUTH SUBSALICYLATE. Presented by DR CHARLES ALBERT SHUMATE for DR HARRY E ALDERSON

This patient was presented at the meeting of this society in December 1934 with the diagnosis of lupus erythematosus resistant to therapy with a gold, but responding to treatment with a bismuth preparation (ARCH DERMAT & SYPH 32 311 [Aug] 1935). At that time there was discussion as to whether the disorder was syphilis, sarcoid or lupus erythematosus. Serologic tests were negative, the history was irrelevant, the results of biopsy suggested lupus erythematosus. The treatment had consisted of nine intravenous injections of 5 mg of gold sodium thiosulfate at weekly intervals, and during the period of treatment the eruption on the face became steadily worse. Injections of gold sodium thiosulfate were discontinued, and eight injections of 2 cc of bismuth subsalicylate were given. The patient improved until, at the time of the meeting, only slight involvement remained. Wassermann tests have been repeatedly negative, and biopsy by Dr Ingels has revealed "lupus erythematosus showing features of sarcoid."

The patient was again presented before the society in March 1935 (ARCH DERMAT & SYPH 32 987 [Dec] 1935), after having received seven weekly injections of neoarsphenamine. The lesions had reappeared and extended over a more extensive area than when the patient was first seen.

Then nine intramuscular injections of 2 cc of bismuth subsalicylate were given at weekly intervals. The face cleared entirely, and it has remained free from lesions. The lesions started to clear after the third injection. No local remedies were used.

EPIDERMOLYSIS BULLOSA Presented by DR MERLIN MAYNARD, San Jose, Calif

This 5 month old baby is presented with a diagnosis of either epidermolysis bullosa or pachyonychia congenita. The history is as follows. Both the mother and grandmother have always had skins that blistered easily. For example, a wrinkle in a girdle caused a blister on the skin. Otherwise the family history is irrelevant.

At the time of birth blisters were noticed on the child's fingers. When the child was 3 days old these lesions were considered impetigo contagiosa and were treated as such. The baby was seen once by Dr H J Templeton, who examined the lesions for thrush but found no fungi. The child was then in the St Helena Sanitarium and Hospital, Sanitarium, Calif, for five weeks, where he was treated for impetigo. The baby has had thrush in the mouth throughout the disease. When I first saw the patient, on Aug 23, 1935, definite lesions of impetigo contagiosa were present together with other lesions. The mother also had impetigo. However, I was surprised to find that the skin peeled to its full thickness and that bleeding occurred when a lesion was opened. As a result of treatment the impetigo has completely disappeared, but blisters containing clear fluid and not showing

evidence of inflammation continue to develop at all points of friction—such as the tips of the fingers, the elbows and the heels—after the application of adhesive tape, and from wrinkles in the bandages. Horny plugs, like small corns, have formed on the heels. No evidence of thrush has been found in the lesions. Nikolsky's sign is positive.

DISCUSSION

DR MERLIN MAYNARD, San Jose, Calif. I was much interested in an article on pachyonychia congenita by A. W. Sohrweide in this month's issue of the ARCHIVES (32:370 [Sept.] 1935). I have little doubt about the correctness of the diagnosis of epidermolysis bullosa, but I was interested in the fact that in this article it is stated that many features of this condition are also found in patients with pachyonychia congenita.

When the mother brought the child for examination she told me that the hands and feet sweated considerably. One finds the same thing in patients with pachyonychia congenita. The earliest occurrence reported was in a child aged 3 years. There has been no report of the occurrence of the disease in an infant.

I wonder whether pachyonychia congenita will develop in this child or whether pachyonychia congenita is a form of epidermolysis bullosa.

As far as treatment by the use of anterior pituitary is concerned, I wonder what might be a safe dose. I do not want to bring on precocious puberty, and I do not know what the effect in a child as young as this would be. I should appreciate suggestions as to diagnosis, treatment and dosage.

DR H. J. TEMPLETON, Oakland, Calif. To me this is the most interesting condition presented this evening, partly because I saw the patient several months ago for just one observation. At that time the baby had definite thrush of the mouth and pustular lesions of the body. Frankly, I did not think of a diagnosis of epidermolysis bullosa at that time. I was thinking instead of pyoderma or cutaneous thrush. I made cultures for thrush, but there was no growth. I have no experience with epidermolysis bullosa in infants and am not prepared to offer a diagnosis.

PARAPSORIASIS EN PLAQUES (BROCC) Presented by DR W. M. MEININGER for
DR A. E. INGELS

J. E., a man aged 65, single, a native of Sweden, complains of a rash on the body, which has been present for over one year. He first noticed "spots" on the chest. They have caused no discomfort but have gradually spread over the trunk and upper extremities. There is no history of exposure to excessive heat. The patient had no previous similar eruption, and he makes no other complaints.

He had typhoid in childhood and suffered an injury to the skull, possibly a fracture, in 1912. He has had no venereal disease.

There are yellowish-brown, fairly well defined plaques about the size of a walnut on the trunk and upper extremities. Fine, adherent, almost imperceptible scales are present. The lesions are not infiltrated. There is an erythrosquamous eruption on the dorsa of both hands. Dentition is poor, there are many crowned and some devitalized teeth. Other results of physical examination were essentially negative.

The Wassermann reaction of the blood was negative. The blood count gave normal results. A biopsy was made. Dr. Ingels will present sections.

The diagnosis is parapsoriasis en plaques (Brocq).

DISCUSSION

DR W. M. MEININGER. We have not treated the patient, but apparently he has used some remedies which are responsible for the erythematous areas. I think that the duration of the lesions, their character and the lack of infiltration and of subjective sensation justify a clinical diagnosis of parapsoriasis.

DR A E INGELS The sections show a mild nonspecific round cell infiltration. There is nothing characteristic so far, although it seems that one can exclude some possibilities which have to be considered in this case. The absence of plasma cells excludes syphilis. The absence of migration of leukocytes and the absence of micro-abscesses seem to exclude psoriasis. The appearance of the sections excludes simple neurodermatitis and pityriasis rosea.

Because I wondered about the correctness of the diagnosis I should like to throw some doubt on the results of treatment of parapsoriasis. Dr Chipman has reported the cure of parapsoriasis by local applications, and I understand that some dermatologists believe that anthralin (di-hydroxyanthranol) effects a cure. Was the diagnosis correct in the cases which Dr Chipman reported, and is it beyond doubt in this case?

DR G V KULCHAR To me the diagnosis of parapsoriasis has always been a clinical, not a histologic one. Parapsoriasis is a dermatosis in which there occur plaques which are yellowish in the center, as described by Crocker. At least this dermatosis fits into no other classification, and for that reason it has been classified as parapsoriasis.

DR H J TEMPLETON, Oakland, Calif. It is important to differentiate this condition from the premfiltrative stage of mycosis fungoides.

DR HARRY E ALDERSON My co-workers and I have seen this man a number of times, and there was no evidence of itching. He also stated that there was no itching. We have considered the diagnosis of a prefungoid condition, and the disorder may develop into a frank granuloma fungoides, as some of the eruptions diagnosed as parapsoriasis do.

LYMPHOGRANULOMA INGUINALE Presented by DR N N EPSTEIN

P C, a man aged 38, a Lithuanian, a cigar clerk, entered the University of California Hospital on Sept 2, 1935, and was discharged on Sept 27, 1935.

Nine days before admission to the hospital the patient noticed a small abrasion on the dorsal surface of the sulcus. He began to have chills and fever four days later, and simultaneous enlargement of the right inguinal lymph nodes was noted. There is a history of sexual intercourse with a Negress six and twelve weeks before the appearance of the sore.

The patient had a primary sore in 1925, after the appearance of which he received four or five intravenous injections. He has received no treatment since.

A dime-sized ulcer is present on the sulcus, and there is a large tender mass in the right groin. The temperature was 38.2 C (100.76 F). Dark-field examination failed to show *Spirochaeta pallida*. Four more dark-field examinations made while the patient was in the hospital also gave negative results. The Wassermann and the Kahn reactions of the blood were negative on Sept 19, 1935.

The Frei test gave a 4 plus reaction. About 100 cc of pus was aspirated on two occasions. Examination of the blood on Sept 2, 1935, showed 10,250 white cells and 79 per cent polymorphonuclears, on September 5 there were 16,300 white cells and 84 per cent polymorphonuclears.

Treatment has consisted of rest and application of an ice-bag.

The diagnosis is lymphogranuloma inguinale.

DISCUSSION

DR N N EPSTEIN This patient presents an excellent example of lymphogranuloma inguinale, and the fact that the primary lesion was present furnished an opportunity to study it from the beginning.

The amount of fever present was striking. The temperature became normal when free drainage was established. It is unusual that the primary lesion should persist for this length of time.

I wish to ask Dr Levin how accurate he thinks the Frei test is.

DR E A LEVIN Those who have done much work with the disease believe that the test is specific. However, in early stages of the infection it is possible for the Frei test to be negative. In a study of thousands of cases it has been found to be negative in cases of venereal diseases other than lymphogranuloma inguinale. The test apparently may remain positive throughout the patient's life. The longest period reported for a positive test was thirty-nine years, that occurred in a patient with a residual scar.

DR F G NOVY JR, Oakland, Calif We secured 100 cc of pure pus in this case, which we tried to culture for the filtrable virus, and so far the results of the cultures have been negative.

MULTIPLE HEMORRHAGIC FAMILIAL TELANGIECTASIA OF THE SKIN AND MUCOUS MEMBRANE (OSIER) Presented by DR H J TEMPLETON, Oakland, Calif

H D S, aged 23, was first seen at the E V Cowell Memorial Hospital, Berkeley, Calif, about Sept 1, 1935, being referred by Dr Howell of Berkeley. The patient complained of nosebleeds and of pinhead-sized red spots on the lips and face.

There are many pinhead-sized telangiectatic spots on the cheeks, on the lips and on the nasal mucosa. The patient states that his father and brother suffered from the same disorder. A diagnosis of multiple hemorrhagic familial telangiectasia of the skin and mucous membrane was made. Treatment has consisted of destruction by means of electrodesiccation or the actual cautery.

DISCUSSION

DR H J TEMPLETON, Oakland, Calif This is apparently a clearcut case of Osier's multiple hemorrhagic familial telangiectasia of the skin. The patient's father and brother had the same disorder.

I have wondered as to whether or not any such treatment as that which has been used for hemophilia, that is, injection of ovarian substance or of snake venom might be of value in this case.

A CASE FOR DIAGNOSIS (IODODERMA?) Presented by DR H J TEMPLETON, Oakland, Calif

Mr S J D, aged about 65, presented himself on Aug 19, 1935, because of many papulopustular necrotic lesions on the trunk. The lesions vary from small red papules 3 mm in diameter to pustular and necrotic areas from 3 to 5 mm in diameter and to acneform cystic lesions about 1 cm in diameter. As the necrotic lesions heal, some scarring remains.

The patient had been taking potassium iodide before the onset of the eruption. The Kline test was negative. A differential blood count showed 11,525 white cells, 70 per cent polymorphonuclears, 26 per cent small lymphocytes, 1 per cent large lymphocytes and 3 per cent eosinophils. An intradermal test with tuberculin was strongly positive.

In making the diagnosis, iododerma and papulonecrotic tuberculid were considered. Daily intravenous injections of a 2 per cent solution of sodium chloride have produced only a moderate degree of improvement in a month. The section which is presented shows a picture compatible with papulonecrotic tuberculid.

DISCUSSION

DR G V KULCHAR I think that iododerma is well ruled out. There are no lesions over the face. The character of the lesions suggests acne scrofulosorum or tuberculid.

DR HARRY E ALDERSON I think that a diagnosis of some form of tuberculosis can be established. Has auto-inoculation been tried?

DR A E INGELS I wish I had seen some other sections stained for acid-fast bacilli and elastic and connective tissue I did not see any foci of caseation, the absence of such foci would be absolutely against a diagnosis of papulonecrotic tuberculid The absence of acanthosis practically excludes an iododerma

DR F G NOVY JR, Oakland, Calif I did not feel that the disorder was an iododerma or a papulonecrotic tuberculid The pustules are clearing much faster than papulonecrotic tuberculids ordinarily do

DR MERLIN MAYNARD, San José, Calif I considered the condition to be acne cachecticorum or acne conglobata The tuberculids are often more solid than this lesion

URTICARIA PIGMENTOSA IN AN ADULT Presented by DR HARRY E ALDERSON

Mr F W G, a man aged 35, a carpenter, entered the dermatologic clinic of the Stanford University Hospitals on Sept 10, 1935, because of cutaneous trouble which had lasted for "several" years He stated that when he became overheated or when he rubbed the lesions they swelled up, popped up Otherwise no discomfort from the lesions was ever experienced He could not tell whether the lesions vanished completely, to recur as new ones in other locations

A general examination was made by one of the physicians on the medical service, and no abnormalities, except an anal fistula, were found

The personal and the family history are irrelevant

The Wassermann reaction of the blood was negative on September 13

There is a generalized eruption of a maculopapular-nodular character over the trunk and extremities The face, palms and soles are not involved The lesions are ill defined, brownish and discolored, only a few show a more vivid reddish color When rubbed, a number of them become urticarial and raised above the surface of the skin

A biopsy was made on September 12 Sections (stained by the hematoxylin-eosin, silver nitrate, elastin H and Van Gieson methods) are presented for examination

DISCUSSION

DR HARRY E ALDERSON In cases of these disorders the question occasionally arises whether or not the condition is urticaria pigmentosa or urticaria with pigmentation No mast cells were seen, it is true, but it is known that sometimes they are not found, and a later biopsy may show the typical picture

DR A E INGELS I should like to challenge opinion as to this condition, particularly in this case In the sections there are practically no mast cells The outstanding feature is the deep pigmentation of the basal cell layer and prickle cell layer I should like to hear the members' opinion regarding the sections

DR MERLIN MAYNARD, San José, Calif I looked at the sections It is true, of course, that there are many cases in which the clinical picture is that of urticaria pigmentosa and in which sections do not show mast cells The pathologic picture is lacking in the one characteristic which establishes a diagnosis of urticaria pigmentosa

A CASE FOR DIAGNOSIS Presented by DR H V ALLINGTON for DR C J LUNSFORD, Oakland, Calif

Mrs M was first seen on September 19 because of hypertrophy and tenderness of the soft tissue overlying the hard palate in the area covered by a partial plate which she has worn for the last ten years The affected tissue is thrown into deep rugae, with individual islands of tissue resembling lymphangiomatous tissue

The condition was first noted, from three to four months ago, because of the discomfort which it caused, and the patient has been somewhat more comfortable since her plate was adjusted by her dentist The condition has improved somewhat since the plate was removed entirely

DISCUSSION

DR H V ALLINGTON My co-workers and I believe that the disorder represents a reaction to irritation from a plate. In a conversation with a dentist about this condition I was told that he had seen it in several patients. He suggested as treatment the accurate fitting of plates and the wearing of metal rather than of rubber plates. He expressed the opinion that rubber may cause degeneration and sluggishness of the tissues because, being a poor caloric conductor, it deprives the tissues of the stimulating effects of heat and cold.

DR L R TAUSSIG Has any attempt been made to find out whether the patient is sensitive to hard rubber?

DR H V ALLINGTON A patch test was made, and no sensitivity was found. Temporary relief followed the removal of the plate.

RADIATING TELANGIECTASIA OF THE LOWER PORTION OF THE LEGS Presented by DR C J LUNSFORD, Oakland, Calif

This woman, aged about 25, presents on the extensor surfaces of the lower portions of both legs and on the ankles, running down onto the dorsa of the feet, superficial spreading small blood vessels, which form a network. In some places there appears to be a central blood vessel from which the small branches extend. Altogether the appearance is that of a large spider nevus.

The patient states that the telangiectasia has been present for years. She states that it is not present in the morning when she awakens but that it immediately appears when she steps on her feet.

There are no subjective symptoms. Aside from some enlarged varicose veins, no abnormalities are known to be present.

RADIATING TELANGIECTASIA OF THE LEGS Presented by DR H V ALLINGTON

Miss C, a Portuguese woman aged 38, is presented with a diagnosis of radiating telangiectasia of the legs. The patient has a diffuse telangiectatic network over the lower third of each leg and ankle, which began about ten years ago and has slowly become more extensive.

The patient had measles and mumps in childhood. She often suffered from sore throat before she underwent a tonsillectomy at the age of 25. Since 1928 she has had frequent spells of tachycardia, fatigability and mild precordial pain. Careful studies of the heart have failed to reveal any chronic abnormalities, although there is a slight right axis deviation in the electrocardiogram, and a periodic slight cyanosis has suggested the presence of some mild congenital cardiac anomaly, such as a partially patent foramen ovale or ductus arteriosus. There is mild swelling of the ankles during hot weather. The patient also suffered from pain in the right lower quadrant of the abdomen for several years, after a laparotomy was performed a year ago, at which time a chocolate cyst over the right ovary was removed, the pain disappeared.

Extensive laboratory work has given negative results. The patient has felt somewhat better since she took thyroid, although in 1928 her basal metabolic rate was reported as +14 per cent.

DISCUSSION

DR H J TEMPLETON In the past ten years my co-workers and I have observed six or eight cases of this condition, which fits in, I believe, with what is described by Edel as radiating telangiectasia of the legs (*Brit J Dermat* 38:112 [March] 1926).

DR ORLAND F MONTGOMERY In the cases I have observed the lines have converged into the ankle.

DR G V KULCHAR I disagree with the diagnosis as presented. The radiating type of telangiectasia with which I am acquainted is more like a spider nevus, radiating in various directions. These lesions, to my mind, conform to the syndrome

described by Parkes Weber. Such lesions are usually due to exposure to the elements. I think he called the disorder erythrocyanosis puellorum.

DR H V ALLINGTON. One of the two patients had a thorough examination. It is believed that there is some possibility of a congenital cardiac lesion in this patient, although it has been impossible to prove the existence of such a lesion.

DR HARRY E ALDERSON. A young woman whom I saw on a hike in the high mountains jumped into a pool of ice-water in the evening after a long climb. Telangiectasia of this character promptly followed.

A CASE FOR DIAGNOSIS Presented by DR ORLAND F MONTGOMERY

A Y, a woman aged 23, single, a Japanese, states that except for a scaly scalp she had always been well until March of this year, when a weeping eruption developed about the ears and nostrils. Within a week an almost complete alopecia resulted. There is no history of fever. The eruption later extended to the pubic region, axillae and thighs. Menstruation, which was formerly normal, has been completely suppressed save for a normal period early in August. The patient complains that her skin has always been dry.

When the patient was seen first, in July, there were (1) general ichthyosis, which was mild, (2) almost complete universal alopecia, (3) moist and vegetating massive dermatitis, noteworthy because of its complete symmetry, about the ears, nose, axillae, pubic region, inner and dorsal aspects of the thighs and dorsal aspects of both feet.

The impression was that the patient was suffering from a debilitating and wasting disease.

Laboratory examinations revealed nothing noteworthy save a hemoglobin content of 70 per cent, a corresponding reduction in red cells and a color index of 1. There were changes in the size and shape of the red cells suggesting a primary anemia. The basal metabolic rate was not determined.

DISCUSSION

DR ORLAND F MONTGOMERY. This patient is presented for diagnosis and therapeutic suggestions. I cannot find a diagnosis that fits the disorder. Under treatment the eruption was clearing up, but it recurred. The eruption was above the umbilicus at one time. The eruption below the waist cleared up almost entirely and then recurred. When it was first seen it was tremendously vegetating, the lesions having almost a cauliflower-like appearance. From the appearance of the lesion around the scalp some one suggested the diagnosis of psoriasis. No fungi have been found.

I think that this patient is definitely ill and has been ever since I have seen her. She has had some form of avitaminosis. Because of the complete symmetry of the eruption I am inclined to believe that it is constitutional. I should be surprised to see a seborrheic lesion as symmetrical as that. I spoke to a neurologist about the case, and he thought that the disorder might be a trophic disturbance.

DR HARRY E ALDERSON. Have experiments with auto-inoculation been tried?

DR ORLAND F MONTGOMERY. No such experiments have been made.

DR HARRY E ALDERSON. The well defined character of the main process and the sharply defined outlying islands suggested to me, as they did to Dr Montgomery in the beginning, that the disorder might be a mycotic process. I suppose the patient has tried a great deal of home therapy?

DR ORLAND F MONTGOMERY. No, I do not think she has. As to food, she has had an average diet. It is known that the Japanese are much inclined to have eczema.

DR H V ALLINGTON. The lesions look like those reported by Hopkins to be due to infection with a yeast. In his cases, I believe, he considered the possibility that an intestinal infection due to a yeast was responsible for the symptoms.

DR MERLIN MAYNARD, San José, Calif I have observed two cases of disorders similar to this Both occurred in young Italian girls shortly after puberty In both girls the disorder began with lesions behind the ears, these were followed by a generalized eczematoid dermatitis such as is presented by this patient I got nowhere as far as treatment was concerned in either of these cases, except for bringing about temporary relief, as Dr Montgomery has done

My opinion is that the disorder is probably a sensitivity of the skin to staphylococci I think also that the theory that an avitaminosis is responsible is a good one To one girl I gave viosterol, but it did no good To the other I gave iron and ammonium citrates, and that did no good either The girls were both chloremic In one the hemoglobin content of the blood was 55 per cent

DR G V KULCHAR The distribution, the well defined border and the character of the lesion, in addition to the prostration—the whole picture—make the diagnosis of pellagra certain

FAVUS Presented by DR N N EPSTEIN

S Z, a woman aged 21, was born in Illinois but has lived in Modesto, Calif, since early childhood Her condition dates back about ten years, when a slowly progressive loss of hair with scaling and crusting was noticed about the scalp A change in several nails of each hand occurred, causing discoloration and brittleness of the involved nails

The patient was first seen in March 1930, when scarring and scutula were present in numerous areas throughout the scalp These have gradually extended The involvement of the finger-nails has progressed slowly

Microscopic examination of involved hairs showed mycelial threads along their long axis Culture confirmed the diagnosis of infection with *Achorion Schoenleini*

DISCUSSION

DR N N EPSTEIN This patient has been under my observation for four years The condition has progressed slowly, gradually involving a large part of the scalp The inflammation about the hair follicles is slight, considering the amount of fungus found in the lesion

The patient has lived in Modesto, Calif, and is a white girl She has not been under constant observation for longer than a couple of weeks at a time I should like to know the members' opinion as to prognosis at the present time

DR STUART C WAY Several months ago I discussed this case with Dr Epstein and suggested that the lesions, a few at a time, be lightly treated with phenol and that the following formula be applied once daily to the entire scalp thymol, 2 Gm, iodine crystals, 12 Gm, turpentine, 20 cc, olive oil in quantity sufficient to make 60 cc

LUPUS ERYTHEMATOSUS RESISTANT TO INTRAVENOUS ADMINISTRATION OF A GOLD PREPARATION BUT RESPONDING TO INTRAMUSCULAR ADMINISTRATION OF A BISMUTH PREPARATION AND TO A VEGETABLE DIET Presented by DR A E INGELS

Mr H H, aged 50, a janitor at the Laguna Honda Home Infirmary, has been treated at the outpatient clinic of that institution since November 1933 His lupus erythematosus had lasted from twelve to fifteen years, according to the note on his treatment sheet Presumably his disorder involved the entire face, the ears and some parts of the scalp

This patient was seen first as an outpatient and has been observed for two years Dr Epstein has seen him intermittently, and he and I have seen the patient for approximately one year each He has received in all fifty-eight injections of a gold preparation, with strikingly little effect He would improve for a short while, but the condition would recur

I finally thought that bismuth should be tried, and I also ordered a vegetable fat diet. The patient has received six weekly injections so far, and marked improvement started within fourteen days.

DISCUSSION

DR N N EPSTEIN When I first saw this patient he had extensive lupus erythematosus, and I believed that treatment with a gold preparation had resulted in about 50 per cent improvement. The condition remained stationary between courses of treatment with the gold preparation. Certainly his appearance tonight is entirely different from that which he presented when I last saw him. The lesions are much more superficial than in most cases of lupus erythematosus. I agree with Dr Ingels that in this case bismuth certainly has done a great deal for the patient.

DR H J TEMPLETON, Oakland, Calif I should like to make one remark about the dosage of gold and sodium thiosulfate. Physicians have been rather cautious of late about dosage and have not administered more than 100 mg. Recently, however, my co-workers and I treated a patient with discoid lesions of the face in whom conservative doses produced no benefit. Increasing the dose to 250 mg per week has caused all of the lesions to disappear. He is the only patient to whom we have given such large doses.

DR STUART C WAY The use of preparations containing bismuth is not new in the treatment of lupus erythematosus. An excessive amount of fibrosis, however, renders it less efficient.

DR A E INGELS I was much interested in Dr Templeton's remark about dosage. Expert dermatologists in Germany have expressed almost unanimously, in a resume of the subject, the opinion that the dose should be as low as possible. That reminds me of a patient to whom 100 mg was given by mistake, causing an almost fatal flare-up of the disease.

DR L R TAUSSIG It was interesting this summer to hear a paper on the subject by Wright, who is associated with Schamberg's clinic. He has used doses from 100 mg up as a routine. It was interesting, however, in going over a considerable series of his cases to find that he had two fatalities which could be traced to the toxic effect of the gold preparation and that at least 25 per cent of the patients showed toxic symptoms. I think that that report alone would make one hesitate to resort to large doses. In the French literature there are many reports of toxic eruptions due to gold preparations, evil results being apparently more frequent than with nearsphenamine. That, I believe, is due to the fact that French physicians have used doses much higher than those administered in this country.

DR STUART C WAY In 1922, when I used gold in the form of krysolgan, the doses were usually larger, and the reactions were severe indeed.

KERATOSIS PILARIS Presented by DR N N EPSTEIN

M M, a man aged 24, was first seen in August 1933, at which time he complained of an extensive erythematofollicular eruption over the trunk and arms. The lesions consisted of acuminate papules situated about the hair follicles. There were no associated symptoms. The condition has remained the same during the past two years, altogether it has been present about four or five years.

DISCUSSION

DR N N EPSTEIN This patient is presented simply because of the extent of the condition.

DR ORLAND F MONTGOMERY I disagree with the diagnosis. The arms and legs are quite free from eruption. The distribution plus the degree of inflammatory reaction leads me to believe that the disorder is not keratosis pilaris.

Monilia also attacks the lungs, causing fibrosis and perhaps asthenia and death. If this is treated early with iodides the prognosis is better.

A CASE FOR DIAGNOSIS Presented by DR M W RUBENSTEIN

J S, a girl aged 6½ years, about five weeks ago complained of pain in the abdomen. A local physician gave her a liquid diet. The physical examination at that time apparently gave negative results. The patient's appetite remained good. She was then put on a limited liquid diet and was given medication by mouth. About three weeks ago an eruption appeared on the abdomen and back. Within a few days it spread to the palms and soles, consisting at that time of pruritic papules. Within the past few days bullous lesions have appeared on the palms and soles. The pain in the abdomen lasted for about two weeks. During the first two weeks of illness the temperature fluctuated between 99 and 100 F. Lately the child has complained of soreness of the finger-tips.

DISCUSSION

DR B A GOLDMANN I believe the disorder is toxic erythema which possibly began as an acute dermatophytosis of the palms and soles.

DR STANLEY CRAWFORD I think that this is a case of acrodynia. This diagnosis is suggested by the characteristic flaccid posture of the child, the so-called "pretzel position." I admit that not all the classic signs, such as pain, fretfulness, etc., are present, but the mother stated that the child had complained of severe itching of the palms and soles. It may be too early for these classic signs to be present, or they may not appear at all.

DR. M W RUBENSTEIN I saw this patient for the first time this afternoon. I cannot consider the diagnosis of acrodynia. A child with acrodynia is fretful, cries and whines all the time, does not want to eat, is cold and clammy and has painful hands. The patient does not show these signs.

NOTE—The patient was sent to the hospital and was apparently getting well. After she had been in the hospital for three weeks she died suddenly, there was no apparent cause of death. Permission for autopsy was not obtained.

A CASE FOR DIAGNOSIS (MYELOID LEUKEMIA?) Presented by DR H T PHILLIPS, Wheeling, W Va, and J C KERR, McKeesport, Pa

Mr G E, aged 38, complains of a papulonodular eruption of several years' duration. The color is from normal to reddish brown, and the involvement is symmetrical and generalized. Periods of regression and of exacerbation have occurred, and occasionally itching has been intolerable, at other times there have been no subjective symptoms.

The patient was in a sanatorium in 1929 for pulmonary tuberculosis, during his sojourn there roentgenograms showed tuberculous involvement, but examination of the sputum never gave positive results. Cutaneous lesions appeared first while the patient was in the sanatorium. The Wassermann and the Kahn test were negative. A blood cell count on Aug 23, 1935, showed 3,610,000 red cells, 57 per cent hemoglobin and 12,450 white cells. The results of the differential count were as follows: polymorphonuclears, 66 per cent, small lymphocytes, 26 per cent, large lymphocytes, 7 per cent, eosinophils, 1 per cent. Biopsy showed a picture resembling that of myeloid leukemia.

Another blood count, on Sept 17, 1935, showed 75 per cent hemoglobin, 3,760,000 red cells and 9,500 white cells. The results of the differential count were as follows: polymorphonuclears, 60 per cent, small lymphocytes, 26 per cent, large lymphocytes, 7 per cent, eosinophils, 2 per cent, transitionals, 2 per cent, large monocytes, 3 per cent.

The patient has received four roentgen treatments of one-half erythema dose to the anterior aspect of the right thigh, smoothing of the lesions and disappearance of the itching have resulted.

DISCUSSION

DR. FRANCIS TORREY This child lived in the San Joaquin Valley for one and a half years. She has been in San Francisco for three and a half years. Four years ago she complained of pain in the region of the lower right ribs which continued until she entered the hospital in July 1935. In April 1935 she could not walk because of severe pain in the right hip. Roentgenograms showed involvement of the pelvis and of one rib.

DR. N. N. EPSTEIN I think it is interesting that roentgenograms were the first means of examination that led to a diagnosis.

DR. L. R. TAUSSIG What were the roentgenologic characteristics of the involvement?

DR. N. N. EPSTEIN I could not say exactly. The appearance was similar to that of tuberculosis but not exactly like it.

DR. C. E. SCHOFF, Sacramento, Calif. Dr. Jacobsen reported a case which occurred in Los Angeles in which there was a primary pelvic involvement. It would be interesting if it could be determined whether this patient's infection was primarily in the pelvis.

PITTSBURGH DERMATOLOGICAL SOCIETY

JOSEPH J. HECHT, M.D., *Secretary*

Sept 19, 1935

EMERSON GILLESPIE, M.D., *President*

MONILIASIS Presented by DR. STANLEY CRAWFORD

C. P., a Negro boy aged 10 years, has a marked involvement of the lingual and buccal mucosa with whitish patches producing a downlike appearance due to infection with *Monilia*. The first and second finger-nails of the right hand are thickened, dystrophic and dirty brownish, and the two fingers show a padlike paronychia. Cultures made by Dr. Moore, of St. Louis, revealed *Saccharomyces albicans*.

The child has received iodides. On one occasion a bullous erythema multiforme developed. At present there are rounded, dusky red purpuric macular lesions due to the iodide on the arms, legs and trunk. The vertex of the scalp is entirely covered with amber crusts. Crusting is also present over the bridge of the nose and in the angles of the mouth, and there is an acute purulent conjunctivitis.

DISCUSSION

DR. C. B. NORRIS, Youngstown, Ohio. I should like to know if the diagnosis was reached before the culture was made and how the nails became infected?

DR. F. M. AMSHEL. At first glance the lesions on the legs appeared to have the color typical of an eruption due to phenolphthalein, and I thought that the disorder was caused by that drug. The remains of the bullous lesions on the hands can be seen, and these together with the history of ingestion of iodides make it probable that the condition is an eruption due to iodide.

DR. STANLEY CRAWFORD. In answer to Dr. Norris' questions I wish to state that the tongue showed typical whitish patches. The neighboring mucosa also showed the whitish patches. The fingers involved were the thumb and the next finger of the right hand, the two fingers which the child would most likely put in his mouth. There was also a red paronychia of these fingers. This was quite stubborn and failed to respond to many treatments which were tried. I shall try application of gentian violet and shall report at a future meeting as to results.

ERYTHEMA NODOSUM WITH LESIONS ON THE FACE Presented by DR H T PHILLIPS, Wheeling, W Va, and DR J C KERR, McKeesport, Pa

Mrs R F, aged 36, presents nodular, pink to bluish lesions on the anterior and lateral surfaces of each leg. In addition, she has indurated lesions over the forehead, nose and cheeks. The eruption has been present for two weeks. There is no history of previous illness, but the patient has complained of slight pain in the wrist and elbows since the eruption began.

DISCUSSION

DR H T PHILLIPS, Wheeling, W Va. I did not know what to call the condition on the face, but probably it should be considered a part of the general condition.

JOSEPH J HECHT, M D, *Secretary*

Oct 17, 1935

EMERSON GILLESPIE, M D, *President*

A CASE FOR DIAGNOSIS (LEPROSY?) Presented by DR M W RUBENSTEIN and DR M PETTLER, Beaver Falls, Pa

W H, a married man aged 60, was seen by Dr Rubenstein on May 28, 1935, at which time he presented lesions that resembled a dermatitis due to phenolphthalein or possibly mycosis fungoides. At that time he also presented atrophy of the muscles of the thenar eminence of the left hand and of the left interosseal muscles. Both ulnar nerves were enlarged. The patches of dermatitis were hyperesthetic rather than anesthetic.

Dr J A Mitchell stated that the illness began in June 1934. At the onset there were severe chills, high fever and profuse sweating. The history revealed that the patient had malaria while he was in the Spanish-American War in the Philippines. Physical examination in August 1934 gave the following results: The heart beat was irregular, the temperature was 100 F, the pulse rate was 88, the abdomen was distended, the liver, kidneys and spleen were not palpable, there was intense cyanosis of all the fingers and toes, of the lobes of the ears and of the tip of the nose and edema of several fingers and toes approaching a wet type of gangrene. In addition, there were purpuric spots on the arms and legs varying in size from that of a 5 cent to that of a 50 cent piece. The patient was semicomatose. He was treated at that time by administration of digitalis and thyroid, forcing of fluids and injections of dextrose. Within a few days the cyanosis improved with exception of that of four toes of the left foot, three toes of the right foot and two fingers of the left hand. In the process progressed to a dry gangrene and loss of the terminal phalanges. There was very little pain. In February 1935 a macular eruption associated with a marked stinging and burning sensation developed over the entire body, especially over the back. The patient stated that he had taken phenolphthalein occasionally. Ingestion of phenolphthalein was discontinued, and the lesions progressed to an indurated stage.

Examination of the blood on Nov 4, 1934, showed 4,400,000 red cells and 8,900 white cells. The results of the differential count were as follows: polymorphonuclears, 71 per cent, lymphocytes, 20 per cent, monocytes, 4 per cent. The Wassermann and the Kahn test and cutaneous tests with quinine salts were negative. Examination of fresh blood for parasites gave negative results. Examination of the urine showed a 2 plus reaction for albumin and a negative reaction for sugar. The specific gravity was 1.015, there were no casts.

Biopsy of two specimens was reported to show chronic granulomatous infiltration.

DISCUSSION

DR F M AMSHEL I thought, at first glance, that I saw flat, shiny angular papules resembling lichen planus or even a vesicular lichen planus, but of course the fact that the lesions are nodular made me change my mind

DR B A GOLDMANN Have any abnormal cells been seen in the smears? I wish Dr Phillips would send me a smear A polychrome stain would show the different cells

DR F M JACOB Immature cells respond to roentgen radiation, and since in this case the disorder has responded to radiation some immature cells must have been present

DR J C KERR, McKeesport, Pa When we first saw this patient we thought he had leprosy The leonine expression due to the nodular involvement of the ears and face was present, but this occurs also in patients with leukaemia cutis

EPIDERMOLYSIS BULLOSA Presented by DR STANLEY CRAWFORD

K M, a Negro girl aged 12, has had a marked reticulated atrophy over the anterior and posterior aspects of the trunk, buttocks and upper and lower extremities and over the neck and face for the past five years The skin feels dry and shows numerous small rounded scars from bullae which appeared spontaneously There is atrophy of the skin of the body and face The anterior surface of the neck shows numerous scars of bullae The dorsal surface of both hands and of all the fingers is atrophic and shows flaccid bullae which develop after the slightest trauma The tongue is atrophic and shows rounded reddish areas along the sides and anterior portion of the dorsal surface The skin of the eyelids is atrophied, but there is no ectropion

DISCUSSION

DR B A GOLDMANN I believe that this is a case of congenital ichthyosiform erythroderma

DR F M AMSHEL I agree with Dr Goldmann

DR F M JACOB Dr Beinhauer has used theelin in two cases with success The patients were a male and a female

DR STANLEY CRAWFORD There is no ichthyosis in this case There may appear to be on sight, but when the hand is run over the skin it is found to be smooth The skin is atrophic, and this atrophy throws the skin into lozenge-shaped markings Few of the nails are shed I shall try Dr Jacob's suggestion on therapy and shall report the results at a future meeting

ERYSIPELOID Presented by DR H T PHILLIPS, Wheeling, W Va, and DR J C KERR, McKeesport, Pa

Mr E R, aged 25, a butcher, presented purplish-red, flat, smooth lesions with slightly elevated edges over the dorsum of the left thumb and hand, the lesions are of ten days' duration The patient states that he scratched the back of the thumb while cleaning poultry three days before the eruption appeared There is slight itching, but no constitutional symptoms are present

DISCUSSION

DR H T PHILLIPS, Wheeling, W Va I spent my vacation last summer at a resort where crabs are plentiful I asked a fisherman whether they get bitten often He said that they did and that occasionally blood poisoning, which is evidently an erysipeloid, resulted The crabs perhaps get hold of some stale meat The fisherman said that he applied poultices to the arm and that in two weeks the disorder generally got better I believe that if nothing is done the eruption will heal

DR M B GOLDSTEIN, Youngstown, Ohio I believe that Dr Rubenstein's patient also shows signs of hyperthyroidism

DR M W RUBENSTEIN This case is particularly interesting to me because it represents one of the several at least precipitating factors in the cause of pellagra

SUBACUTE FOLLICULAR DERMATITIS (VITAMIN A DEFICIENCY?) Presented by
DR G J BUSMAN and DR F A HEGARTY

G S, a man aged 48, when first examined a month ago had a generalized follicular papular pruritic eruption The skin had a distinct nutmeg grater feel There were no lesions over the proximal phalanges No systemic signs or symptoms were present A Wassermann test of the blood, total and differential blood count, urinalysis and roentgen examination of the chest gave negative results The patient's diet has been somewhat deficient but not abnormally so

Biopsy showed chronic dermatitis and chronic folliculitis The sections were not good, however, the lesion was a true dermatitis It was nonsuppurative, was suggestively granulomatous, and involved the corium and hair follicles There was very little change in the epidermis

DISCUSSION

DR F M JACOB Infants exhibit a papular condition of the skin resulting from too much vitamin A Conversely, there exists a condition arising from the lack of that vitamin Dr Pettler reported that two patients with pityriasis rubra pilaris improved on vitamin therapy I wonder whether there is any relation between the two conditions

DR G J BUSMAN The patient lived in a poor environment and on a poor diet He reported at a hospital and was given a prescription for capsules containing vitamins A, B and D He did not take the capsules, but he did correct his diet as advised, and improvement resulted

PERSISTENT ERUPTION DUE TO IODIDE Presented by DR G J BUSMAN and
DR F A HEGARTY

M H, a woman aged 77, presents bluish-red, irregular nodules from the size of a split pea to that of a walnut on the fingers and on the extensor surfaces of forearms, elbows and legs These lesions began to develop five years ago, since their appearance the patient has been subject to periodic attacks of a generalized papulopustular eruption

When she was first examined by us, in November 1934, she presented the nodular lesions as described and a generalized inflammatory papulopustular eruption on the trunk and extremities There was a history of recent ingestion of potassium iodide, and the history disclosed that the patient had been taking iodized salt for several years

She was hospitalized and reacted severely to a test with 15 minims (0.92 cc) of saturated solution of potassium iodide The generalized picture responded readily to the intravenous injection of physiologic solution of sodium chloride The nodular lesions which are present today have resisted all methods of treatment

Examination of the urine for iodides gave negative results The blood count showed 85 per cent hemoglobin, 4,020,000 red cells and 9,050 white cells The results of the differential count were normal

Biopsy showed focal chronic suppurative dermatitis and hypertrophy and hyperkeratosis of the epidermis

DISCUSSION

DR F M AMSHEL The patient may be sensitive to iodides, but I think that the condition is xanthoma tuberosum multiplex The color, consistency and location of the nodules point to that diagnosis

DR B A GOLDMANN I agree with Dr Amshel

DISCUSSION

DR G J BUSMAN The diagnosis is consistent with the clinical picture. However, a diagnosis of leprosy should not be made unless the Hansen bacillus has been demonstrated.

DR H T PHILLIPS, Wheeling, W Va I am not willing to accept the diagnosis, although the symptoms, such as loss of eyebrows, hyperesthesia and atrophy of the interossei muscles are indicative of leprosy. The organism has not been recovered although an attempt to isolate it has been made.

DR M W RUBENSTEIN I am sorry that the bacillus has not been satisfactorily demonstrated. Nevertheless, I believe that all clinical evidence points definitely to leprosy as the diagnosis.

The acute exanthem which was present in May and June of this year has practically disappeared. The enlarged ulnar nerves, the alopecia of the outer portion of the eyebrows, the partial alopecia of the parietal and occipital regions, the atrophy of the thenar, hypothenar and interossei muscles of both hands, the loss of several digits of both hands and feet, the nodule on the bridge of the nose and the suggestive leonine facies are sufficient clinical evidence to support the diagnosis.

The patient's physician, in a small town nearby, was reluctant to accept the diagnosis. I shall, however, have more sections studied more carefully, and I shall try to obtain further nasal smears.

PELLAGRA Presented by DR M W RUBENSTEIN

F L, an unmarried woman aged 26, states that she was in excellent health until four years ago, at which time, while she was working in a store, a burglar held her up four times in one week. Immediately after that her appetite became poor and she began to suffer from nausea, vomiting and severe cramps. She weighed 145 pounds (65.8 Kg) at that time. Since then she has taken no food other than milk. The patient has been under the care of a neurologist for the past year because of nervousness, spasms of the stomach, severe pain and colic. He made a diagnosis of paramyoclonus multiplex. The spasms included the abdomen and chest and were severe. Symptoms which had been present for the last four years have now practically disappeared. About five weeks ago a macular eruption occurred around the neck and inner aspects of the arms, this was followed immediately by an eruption on the dorsa of the feet and hands. The patient was unable to retain any food and vomited immediately after eating.

The patient is extremely emaciated, she weighs 83 pounds (37.6 Kg). She presents a Casal necklace. Linear bands of dermatitis are present on the flexor aspects of the arms and forearms, and there is a mild exfoliative dermatitis of both hands, stopping sharply at the wrist. The dermatitis involves the tip of the nose. There is a linear band of dermatitis on the dorsa of the ankles, separated by a band of normal skin. There is also a band of dermatitis above the ankles. The patient complains that pain and swelling are present at times in the areas of dermatitis. There have been no vaginal, crural or perianal lesions or involvement of the mouth and tongue.

DISCUSSION

DR G J BUSMAN The case is interesting in that the manifestations add to the list of disorders due to mechanical or functional obstruction to normal ingestion of food. It is comparable to obstruction due to carcinoma, ulcer or similar involvement of the stomach. I do not think that the paramyoclonus multiplex was related to the pellagra, except so far as it interfered with nutrition.

DR H T PHILLIPS, Wheeling, W Va I have observed a somewhat similar disorder. The patient was given empirically one-half erythema dose of roentgen radiation on the wrists and marked improvement resulted. Vitamin and diet therapy, of course, were also used. Two years later it was learned that that patient had regained good health.

an urticaria-like eruption which would clear up several weeks after administration of bismuth was discontinued. The eruption would return on resumption of bismuth therapy. I think that in this case the disorder may be regarded as an allergic eruption due to bismuth.

DR J R DRIVER Fixed eruptions following the administration of heavy metals are well known. Personally, I have never seen a fixed eruption quite as extensive as that which this patient presents. Eruptions of this type following the use of arsenic are often prolonged by subsequent injections of preparations containing heavy metals, such as bismuth and mercury. I am of the opinion that in this case the disorder is an eruption due to heavy metal which has been kept active by subsequent injections of bismuth subsalicylate.

DR W H CONNOR This patient has been studied from the standpoint of lymphoblastoma. Biopsy revealed none of the characteristics of that disease. Moreover, studies of the blood showed no abnormalities. Extensive cultures for fungi have also been made, all have given negative results. All administration of heavy metals has been discontinued, and the eruption persists, although it is possibly slightly improved. I wish to call attention also to the fact that the arsenical used was mapharsen.

DR JOHN E RAUSCHKOLB I have observed this case since the appearance of the eruption, and I thought for a long time that the disorder was an arsenical dermatitis. I have also more recently thought that there was some suggestion of erythema multiforme or possibly of disseminating lupus erythematosus. Some injections of bismuth subsalicylate were given after the eruption appeared to see whether they accentuated the eruption. My co-workers and I were not sure that there was any particular exacerbation.

NOTE—The patient died of bronchopneumonia in December 1935. Autopsy observations were not helpful in establishing a positive diagnosis of the cutaneous eruption.

A CASE FOR DIAGNOSIS Presented by DR JOHN E RAUSCHKOLB

N T, a woman aged 65, single, from the outpatient department of the City Hospital, has a crusted crescent-shaped lesion, 4 cm in length, on the lower portion of the left cheek. The lesion started three years ago as a small red spot which gradually increased in size. The patient picks at the lesion in order to remove crusts. Examination reveals also a perforated nasal septum and chronic ozena. The Wassermann reaction of the blood was negative.

DISCUSSION

DR H J PARKHURST, Toledo, Ohio One would have to consider the possibility of syphilis. However, the process seems to be rather superficial, and the configuration of the lesion and the history that the patient picks at it a great deal lead me to favor a diagnosis of dermatitis factitia.

DR C L CUMMER I have the same impression as Dr Parkhurst.

DR R E BARNEY I also believe that this is possibly a case of dermatitis factitia on account of the rather acutely inflammatory base with crust formation and the presence of a certain amount of pus. I suggest that dressings moistened with boric acid be used in an effort to clear up the lesion, when it heals the real characteristics may be more apparent.

DR JOHN E RAUSCHKOLB This patient was first seen about one week ago, and the biopsy specimen has not yet been examined. So much improvement has followed the administration of potassium iodide that in my opinion a diagnosis of tertiary syphilis is most probable.

NOTE—Biopsy revealed a basal cell epithelioma, and the lesion healed completely after administration of fractional doses of roentgen rays according to the technic of Coutard.

DR J J HECHT This patient had been at the Pittsburgh Skin and Cancer Foundation At that institution a diagnosis of xanthoma tuberosum multiplex was made and verified by biopsy

DR H T PHILLIPS, Wheeling, W Va Why could not the patient have had the two conditions?

DR G J BUSMAN I agree that the patient perhaps had exanthema tuberosum multiplex, but when she was given the saturated solution of potassium iodide the lesions flared up, bullae developed and the mouth and tongue became sore The patient herself knows that she is sensitive to iodides The saline solution has brought the condition to its present state, but no further improvement can be achieved

CLEVELAND DERMATOLOGICAL SOCIETY

J R DRIVER, M.D., *Reporter*

Sept 26 and Oct 24, 1935

H J MISKJIAN, M.D., *Presiding*

A CASE FOR DIAGNOSIS Presented by DR W H CONNOR

C C, a woman aged 48, from the service of Dr Cole and Dr Driver at the City Hospital, has secondary syphilis and received seventeen injections of mapharsen, or a total of 860 Gm, from June 1934 to Feb 20, 1935 In addition, she received twenty-five intramuscular injections of bismuth subsalicylate A few days after the final injection of mapharsen was given, there developed a generalized pruritic eruption simulating seborrheic dermatitis The patient was given sodium thiosulfate intravenously and by mouth and seemed to improve The administration of bismuth subsalicylate was then resumed The eruption, however, persisted, a moderate exacerbation and partial remission taking place The patient has been hospitalized since Aug 9, 1935

There is a widespread scaly eruption consisting of erythematous patches with scales The lesions are round, vary in size from that of a 5 cent to that of a 25 cent piece and have a tendency to spread at the periphery and to resolve at the center Coalescence of some of the lesions presents an archiform contour There is marked involvement of the palms and soles, associated with desquamation

The Wassermann reaction of the blood was strongly positive when treatment was started On Oct 5, 1935, it was 1 plus The Wassermann reaction of the spinal fluid was strongly positive in June 1934 and again in September 1935, other results of examination were negative The blood count showed 90 per cent hemoglobin, 4,880,000 red cells and 6,400 white cells with 70 per cent polymorphonuclears

A biopsy was reported on as follows "Minimal changes are present in the epithelium There are some flattening of the rete pegs and hyperkeratosis The corium shows a moderate amount of edema, and about the vessels is a scant infiltrate of small round cells of the inflammatory type"

DISCUSSION

DR H J MISKJIAN In this case it would be difficult to rule out the possibility of an arsenical dermatitis, in spite of the fact that several months have passed since treatment with arsenic was given There are certain features about the eruption which suggest the possibility of lymphoblastoma, especially the premycotic stage of mycosis fungoides

DR BENJAMIN LEVINE A deposit of bismuth producing continued absorption might be responsible for this eruption I have seen cases in which there was

DISCUSSION

DR J R DRIVER Sickle cell anemia is common among Negroes I believe that every young Negro with chronic ulcer of the limbs of unexplained origin should have his blood examined for sickle cells

TERTIARY SYPHILIS, DIFFUSE SYPHILOMA OF THE FACE Presented by DR W H CONNOR

J B, a man aged 57, from the service of Dr Cole and Dr Driver at the City Hospital, contracted syphilis in 1917 while he was in the army, he received fourteen injections in his arm He was treated for erysipelas of the face in 1931 The patient states that he has suffered repeated injuries to his nose in his work as a structural iron worker and that his nose has been unusually large for several years The present trouble started approximately six months ago with a scaly spot about the size of a 5 cent piece on the right cheek, and gradually similar lesions developed about the eyebrows and over the nose and upper lip in a more or less diffuse manner, producing marked swelling of the involved areas

A roentgenogram revealed a striking infiltration of the tissues in the region of the eyebrows and forehead The nose also shows this infiltrating process, and in addition there are dilated venules and occasional pustules over the tip of the nose resembling acne rosacea The upper lip and to a certain extent the cheek present an edematous, erythematous infiltration and some areas of atrophy and scarring

The Wassermann reaction of the blood was strongly positive Examination of the spinal fluid gave negative results Roentgen examination of the chest showed some calcified tuberculous scars in the region of the hilus of the right lung There is no evidence of active tuberculosis A test with a 1:1,000,000 dilution of tuberculin gave a 3 plus reaction

Biopsy showed hyperkeratosis of the epithelium, and in the cutis, both in the papillary layer and in the deeper layers, were changes suggestive of tuberculosis Tubercles were present, which tended to coalesce There was evidence of central caseation in some of these areas There was evidence in some areas of round cell infiltration about the vessels, and giant cells were present The entire picture, however, was one of infectious granulation in which syphilis could not be ruled out Stains for tubercle bacilli and *Spirochaeta pallida* gave negative results The patient has received two intramuscular injections of 2 cc each of iodobismitol and three intravenous injections of 0.3 Gm each of neoarsphenamine

DISCUSSION

DR C G LA ROCCO This patient was seen at the Charity Hospital about one month ago, just before his admission to the City Hospital At that time his condition was considerably different, in that there was more acute inflammation and more edema This process seemed to be chiefly demarcated about the mouth and chin, and there was evidence of some vesiculation on the surface As there was a rise in temperature of over 1.5 F, it was believed that he had erysipelas superimposed on some other condition

DR I L SCHONBERG The process, to my mind, corresponds to the rosacea-like tuberculid of Lewandowsky At the border of the eruption one can demonstrate the apple jelly lesions characteristic of tuberculosis

DR R E BARNEY I consider both syphilis and tuberculosis as possible diagnoses Against the diagnosis of lupus vulgaris, however, is the fact that the process started too late in life and certainly would be unusual Furthermore, I should expect to see more scarring if the disorder were tuberculosis In favor of nodular gumma is the serpiginous outline of the eruption as well as the positive Wassermann reaction I do not think that the disorder is acne rosacea-like

ERYTHEMA PERSTANS Presented by DR. R. E. BARNEY

F. E. D., a man aged 36, states that five weeks ago an eruption appeared on the middle portion of the back. He had a similar attack in February 1935, which lasted for five months. This attack involved the middle third of the back. In the median portion of the back are four annular groups of papules varying in size from that of a 5 cent piece to that of a dollar. The borders of these patches are made up of rather superficial small pea-sized pink papules, while the centers are apparently normal skin. Outside the borders are a few similar, satellite papules. The Wassermann reaction of the blood was negative. The blood counts were normal.

A biopsy of material taken from the border of one of the patches revealed normal epidermis. In the corium, particularly in the reticular layer, there was an infiltrate made up of foci of cells of the lymphocytic series. These cells were disposed periglandularly and perivascularly and were uniform in size and shape. There were no mitoses and no plasma or giant cells.

The patient has been given salicylates by mouth.

DISCUSSION

DR. EMERSON GILLESPIE, Canton, Ohio: There is too much infiltration in these lesions to justify the diagnosis of erythema perstans. I favor a diagnosis of granuloma annulare.

DR. R. E. BARNEY: I have considered the possibility of granuloma annulare, but I do not think that there is enough infiltration, and histologically the section did not show the picture of that disease or of sarcoid.

SICKLE CELL ANEMIA WITH ULCER OF THE LEG Presented by DR. E. W. NETHERTON

B. H., a Negro aged 21, states that his father and mother and three brothers are living and well and that none of them has had any ulcers of the legs or chronic illness. Two years ago a small, crusted lesion appeared on the inner surface of the patient's right ankle. This developed into a chronic ulcer, lasting eight months. It then healed, leaving a soft, thin, pliable scar. In June 1934 a similar lesion appeared on the inner surface of the left ankle. This ulcer has not healed. Treatment has consisted of various local applications, eight roentgen treatments and some ultraviolet irradiation.

The patient is well developed and fairly well nourished. Just below the inner malleolus of the left ankle is an irregular, indolent, deep ulcer with well defined margins. The base is granular, grayish and covered with a purulent exudate. For some distance surrounding the ulcer the skin is hyperpigmented and slightly sclerotic. The scar on the right leg also shows hyperpigmentation at the border. There is no evidence of varicosity of the veins. The Wassermann reaction of the blood was negative. The blood count showed 2,900,000 red cells, 111,000 white cells and 58 per cent hemoglobin. The volume of packed red blood cells was 26 cc per hundred cubic centimeters, 57 per cent of normal. There was moderate anisocytosis. The volume index was 0.98, the color index, 1.00, and the saturation index, 1.01. The results of the differential count were as follows: 52 per cent neutrophils, 37 per cent lymphocytes, 6 per cent eosinophils, 4 per cent monocytes and 1 per cent basophils. The icterus index was 4. The platelet count was normal. There was marked sickling of cells in fresh preparations after twenty-four hours.

The diagnosis was sickle cell anemia.

Treatment has consisted of dusting on of boric acid crystals followed by the application of dressing treated with petrolatum and oral administration of reduced iron and, for the past three weeks, of 10 drops of a saturated solution of potassium iodide.

The lesion has improved approximately 50 per cent under treatment.

Biopsy revealed irregular areas of acanthosis, vacuolation of epidermal cells, chiefly in the prickle cell layer, infrequent mitoses, infiltration of lymphocytes and plasma cells in the upper portion of the derma and slight perivascular lymphocytic infiltration

Therapy has consisted of local dressings with mild medicaments

DISCUSSION

DR S S GREFENBAUM, Philadelphia I suggest an alternate diagnosis of granuloma inguinale limited to the glans penis The marked induration present in certain areas of the lesion does not conform to the clinical description of erythroplasia I think it may be well to make a therapeutic test with freshly prepared antimony and potassium tartrate

DR RICHARD S WEISS, St Louis In examining the sections I thought I could detect many of the features that are described as occurring in erythroplasia of Queyrat My co-workers and I have a white patient, aged about 38, who has a similar process, in his case there is not quite as much inflammation, but the histopathologic features are quite similar to those exhibited by this patient There are acanthosis and breaking through the basement membrane and a moderate subepidermal inflammatory infiltration I believe this patient's disorder will turn out to be erythroplasia of Queyrat, and, in my opinion, unless the penis is amputated and the inguinal glands are cleaned out, the prognosis is highly unfavorable

DR MARION B SULZBERGER, New York I agree with the remarks of Dr Weiss, but I should caution against making this diagnosis without both clinical and histopathologic evidence I think that not infrequently one sees lesions of the penis which simulate erythroplasia Not all these lesions turn out to be this rather rare condition One must therefore exercise great care in making the definite diagnosis and in considering the indications for radical therapy Not only the clinical and histologic appearance but the characteristic course are essential to the diagnosis Nevertheless, in this case I agree with Dr Weiss, the clinical history and the clinical and histopathologic picture are all consistent with the diagnosis of erythroplasia of Queyrat

SCLERODERMA WITH SCLERODACTYLIA, HORNER'S SYNDROME FOLLOWING CERVICAL GANGLIONECTOMY

Mr F R, aged 47, is presented through the courtesy of the department of peripheral vascular disease of the department of surgery, Cincinnati General Hospital

He was first admitted to that hospital in 1931 According to the history, the disorder appeared in 1912, beginning as numbness, tingling, cyanosis and cramping of the fingers Each year thereafter the symptoms seemed to increase in severity and extent, the reactions being less intense in the toes The patient fell on the right hand in 1931 but suffered no fracture At that time the entire hand showed extensive cyanosis and partial flexion contracture of the right index finger, there was similar cyanosis, though less marked, in the feet Sensation was entirely normal at that time

The patient said that he used tobacco moderately, smoking one package of cigarets every three or four days He stated that he did not have syphilis He had gonorrheal urethritis at 17 and at 22

In 1931 the entire left stellate ganglion and part of the last cervical and the second dorsal ganglion were removed by Dr Reid and Dr Zinninger Immediately after the operation it was noted that the left side of the face and forehead were not sweating Several hours afterward the left hand became definitely pinker and warmer than the right Constriction of the pupil was noted the next morning The blood pressure in the right arm was 104 systolic and 68 diastolic, in the left arm it was 118 systolic and 70 diastolic On admission some calcification of the pleura was found There were no other abnormalities Five or six

tuberculosis of Lewandowsky, for in that condition the lesions are considerably smaller. I suggest that in addition to preparations of bismuth and arsenic potassium iodide be administered.

DR E W NETHERTON I should subscribe to the diagnosis of syphilis in this case, and the response to the comparatively small amount of therapy given seems to bear out this diagnosis.

DR C L CUMMER I treated a patient with a disorder similar to this several years ago, the symmetry of the process resembled much that exhibited by Dr Connor's patient. My patient's lesion was found to be a gumma and responded well to therapy.

DR J R DRIVER The case is interesting from the standpoint of differential diagnosis. In addition to the diseases that have been mentioned, I believe that clinically one would also have to consider the possibility of leprosy. The infiltration about the eyebrows is suggestive. However, I believe that the disorder is tertiary syphilis, and the positive Wassermann reaction and the response to treatment seem to make that diagnosis unquestionable.

DR JOHN E RAUSCHKOLB The results of the biopsy are interesting. The presence of giant cell formation and infiltration suggesting characteristic tuberculosis illustrates the difficulty that is often encountered in differentiating histologically between tuberculosis and syphilis. The response to treatment during a period of less than two weeks has been remarkable and seems to establish the diagnosis of syphilis absolutely.

COMBINED MEETING OF THE DERMATOLOGICAL CONFERENCE OF THE MISSISSIPPI VALLEY AND CENTRAL STATES DERMATO- LOGICAL SOCIETY

R G SENOUR, M.D., *Acting Secretary*

Ninth Annual Session, Cincinnati, Nov. 16, 1935

SAMUEL GOLDBLATT, M.D., *in the Chair*

ERYTHROPLASIA OF QUEYRAT?^{*}

I H, a Negro aged 38, states that he has had gonorrheal urethritis since 1915. In 1928 he had an acute retention, which was relieved by catheterization. In 1931 he underwent a suprapubic cystotomy. Since 1929, the prepuce and the glans penis have been inflamed.

Before that the patient had no penile lesions of any sort, and he has had no generalized eruption. In 1925 he had a bubo on the right side, which was incised and drained. No history could be obtained of intramuscular or intravenous therapy of any sort and there is no history of syphilis. At various times the patient has undergone incision and drainage for perineal and scrotal abscesses, and in 1932 he had a prostatic abscess.

The cartilaginous-like swelling and redness have remained about the same for the past three years, the inflammation of the glans seems to improve at times.

The Kahn test of the blood has been repeatedly negative. A smear from material from the glans showed no organisms. Dark-field examination and the Frei test gave negative results.

^{*} This and the following presentations were made by members of the dermatological staff of the Cincinnati General Hospital or by members of the Cincinnati Dermatological Society.

SCLERODERMA, ACNE ROSACEA

Mrs M M, aged 34, says that in the early part of 1934 she first noticed on the left thigh a brownish area, this gradually became firmer and soon became devoid of hair. Shortly afterward a similar eruption appeared on the right thigh and on the lower portion of the legs. At the time of admission to the hospital the patient was about three months pregnant. The rosacea had been present for a number of years, periods of exacerbation being associated with the menses and occasionally with certain dietary indiscretions.

The skin shows rosacea of moderate intensity. There are brownish firm atrophic areas 4 by 6 cm on the anterior surfaces of both thighs, the disorder being less marked on the lower portion of the legs. Small patches are present also on the abdomen and on the back of the neck.

Physical examination showed prominent eyes, the thyroid was diffusely palpable, there were no thrills and no tachycardia or other abnormalities.

Urinalysis, the Kahn test, blood counts and differential counts gave normal results. The basal metabolic rate was +2 per cent. Dextrose tolerance tests showed slightly increased tolerance. Roentgen examination of the sella turcica showed no abnormality.

Biopsy showed changes typical of scleroderma.

In spite of the pregnancy, endocrine therapy, with preparations of the thyroid gland, ovaries and pituitary gland was given cautiously for several months, without any results. Treatment of each leg with the inductotherm produced no appreciable results. The patient was then given four treatments with the Kettering hypertherm, the temperature being maintained at from 104 to 105 F for twenty hours. After these treatments there was definite improvement, the lesions becoming much softer. As pregnancy became more advanced it was considered advisable to discontinue all forms of therapy. The patient was delivered of a normal child in October 1935. Since that time she has received no treatment.

DISCUSSION

DR RICHARD S WEISS, St Louis. I was interested in hearing one of the speakers say that in his experience endocrine therapy cures scleroderma. In my experience results have not been as satisfactory. I have seen certain disorders, particularly the localized and morphea types, clear up as a result of treatment with thyroid, but, on the other hand, I have seen the disorders clear up without any treatment or fail to clear up with treatment by any method. I should like to hear Dr Arnsson discuss this more fully.

DR I J ARNSSON, Buffalo. I was referring to the experience of Sellei, not to my own.

DR FRED WISE, New York. I think it is worth while reporting to the members that Sellei at the recent congress in Budapest, Hungary, presented at least three patients with scleroderma who, judging from the histories, did get well as a result of his treatment. He gives not only pancreatic extract but also desiccated stomach and a "shotgun" preparation of iron, mercury and other heavy metals. There is no definite therapy except the administration of pancreatic extract. I was impressed by the cases of scleroderma that Sellei presented. I did not perceive favorable results in cases of Raynaud's disease or of acrosclerosis.

DR MYER W RUBENSTEIN, Pittsburgh. At present my co-workers and I have under observation a patient with generalized scleroderma who has apparently responded to treatment with pancreatic extract. Several months ago this patient presented a generalized scleroderma, and the prognosis at that time was unfavorable. Treatment has consisted chiefly of administration of pancreatic extract orally and an insulin-free pancreatic extract intramuscularly. The response has been favorable. At present there is only a moderate degree of acrosclerosis in both hands.

months after the operation the patient was reexamined and found to be free from symptoms in a portion of the left side, but there were pain, coldness and discoloration in the right hand and in both feet. The Horner syndrome at this time was also rather marked. Measurements of the cutaneous temperature at this time showed an increased temperature on the left side, starting approximately at the middle of the forearm. There was a difference in temperature of 4 or 5 F. In 1933 the patient was readmitted, and at that time it was noted that he had some trophic changes about the fingers of the left hand and that the changes in the forearms were more marked. The calcium content of the blood was 118 mg per hundred cubic centimeters, and the phosphorus content, 42 mg. No changes were noted in the bones of the hand. The patient received 2 cc of a 0.1 per cent solution of pilocarpine hydrochloride hypodermically daily only for about seventeen days, but no improvement resulted.

There is no family history of Raynaud's disease, tuberculosis or syphilis.

The skin shows changes in the extremities as noted. In addition, sclerodermic facies seems to be developing.

Physical examination gave negative results except for chronic prostatitis.

No laboratory examinations have been made recently, studies of the blood when made gave negative results.

No biopsy has been made.

The condition appears to be becoming progressively worse.

Recently treatments with hyperthermia have been employed, but no improvement has resulted.

DISCUSSION

DR. I. J. ARNSSON, Buffalo. In the light of the investigation by Seller, of Budapest, Hungary, it seems advisable to keep these two concepts separate that of true scleroderma and that of what he called acrosclerosis (sclerodactylia). The etiology, prognosis and treatment of the two conditions are quite different. Whereas scleroderma is thought to result from a disturbance of the glands of internal secretion, particularly the pancreas, sclerodactylia, or acrosclerosis, is a vascular disease and has no relation to the endocrine glands. In the majority of Seller's cases of scleroderma the utilization of glandular therapy proved to be successful, whereas the same treatment was entirely unsuccessful in cases of sclerodactylia, or of what he called acrosclerosis. There are some features and laboratory tests which make possible the differential diagnosis of the two diseases.

DR. FRED WISE, New York. I should like to hear the presenter's opinion of the interpretation in more definite terms than the history gives. He used the term scleroderma. I was unable to find any true scleroderma. I saw an acro-asphyxia. Seller described this condition under the name of acrosclerosis, but I did not see much acrosclerosis in this case. My co-workers and I use the term acro-asphyxia for this type of condition and I think that is related to Raynaud's disease.

DR. LEON GOLDMAN, Cincinnati. Recently changes have developed in the face. Palpation of the cheeks shows that the tissues are much more firm than previously. The changes in the forearm have appeared within the last three or four years, and there are changes in the leg, extending to the foot. The changes in the skin include some atrophy. The Horner syndrome has appeared after the ganglionectomy, there is definite miosis of the pupil.

DR. LOUIS A. BRUNSTING, Rochester, Minn. In my opinion this condition is to be considered as distinct from true scleroderma, it represents a form of symmetrical vasospastic disturbance of the extremities of unknown etiology which Seller named acrosclerosis. Raynaud's disease in male patients is extremely rare. When patients with extensive scleroderma were subjected to treatment by sympathetic ganglionectomy my colleagues and I were at first rather optimistic about the degree of benefit that was obtained. Subsequent observation revealed, however, that such radical treatment is hardly justified unless there is a definite preponderance of the Raynaud syndrome.

of that kind to see whether there was disturbance of the biliary tract, not necessarily a stone but disease in that region, the correction of which might produce some relief

DR FRED WISE, New York One does not often see conditions like this, and I think that they should be discussed Pautrier recently wrote a good description of a condition in which he demonstrated nerve fibers within the lesion, so this disorder and Recklinghausen's disease seem to be two diseases in which one can actually demonstrate nerve fibers in the primary lesion That histologic demonstration may account for the itching present in this condition

DR S W BECKER, Chicago Cases of prurigo nodularis are always interesting because of the two opinions concerning them, namely, (1) that the disorder always starts with itching and the patient produces the nodules by scratching, and (2) that the nodules appear first I questioned this woman carefully, and she stated definitely that the itching appeared first and the lesions came afterward, which supports the idea of French authors that the lesions are neurogenic

POIKILODERMA (JACOBI)

Mrs C A, aged 52, was apparently normal until the present condition appeared on the anterior aspect of the thighs thirty-one years ago Since then it has progressively spread, and at present it affects the greater portion of the body, but the hands and face are only slightly involved The skin is pruritic and burns at times The symptoms are worse in winter than in summer The patient has had "heart trouble" for the past ten years, she has suffered from chronic constipation all her life, and she has constant headaches in the parietal region Menstruation is normal and regular The skin appears to clear up during menstruation The patient states that she has had no venereal infection, she induced two miscarriages, one at 18 and one at 19

Scattered over the trunk, neck and extremities, especially on the adductor surfaces, is a diffuse mottled macular pigmentation of the skin, which appears dry and in many places resembles a mild roentgen ray dermatitis Close examination shows dilatation of the superficial capillaries, with many bright red cayenne pepper spots Areas of distinct atrophy of the skin appear as white spots in a retiform network of hyperpigmentation There are numerous small scars on the skin, resulting from scratching and from previous infections

Physical examination showed that the patient was well developed and well nourished, she presented no evidence of muscular atrophy and was not apparently ill The pupils were irregular but reacted to light, other reflexes were normal The buccal mucosa was normal The heart was not enlarged, no murmurs were heard, and the rate and rhythm were normal The blood pressure was 135 systolic and 80 diastolic The lungs were normal Palpation of the abdomen showed no abnormal masses or areas of tenderness The glands were not enlarged Pelvic examination gave negative results The vaginal mucosa was normal

The Wassermann test of the blood and urinalysis gave negative results The blood count showed 4,300,000 erythrocytes, 6,200 leukocytes and 85 per cent hemoglobin The differential count showed 72 per cent polymorphonuclear neutrophils, 24 per cent lymphocytes and 4 per cent eosinophils Roentgen examination of the pituitary fossa showed normal conditions

Biopsy of material from an atrophic area of the skin showed hyperkeratosis, absence of the stratum lucidum and stratum granularum, flattening of the stratum mucosum with loss of rete pegs, fragmentation and degeneration of the collagen and degeneration of the elastic tissue in the papillary and reticular layers, dilatation of capillaries and lymphatics and a rather diffuse infiltration of lymphocytes in the corium

During the three years the patient had been under observation her condition had remained unchanged At one time while she was receiving ultraviolet radiation there appeared numerous pruriginous papules from the size of a pinhead to that of a pea, which biopsy showed to be lymphocytic granulomas

Because of lack of involvement of the exposed portions of the skin the patient was given repeated treatments with ultraviolet radiation, but no improvement in the cutaneous condition resulted Roentgen irradiation of the acutely pruritic

PRURIGO NODULARIS

M G, a Negress aged 54, states that lesions first appeared on the lower portion of the legs thirty years ago and have gradually spread and increased in number until at present the eruption involves all the cutaneous surfaces. There are no lesions on the mucous membranes.

The patient's father and mother never had a cutaneous disorder. She had eleven brothers and sisters, seven lived to adult life. Only one brother had a cutaneous condition. His arms itched intensely at times, but no eruption ever appeared.

The patient is well developed and well nourished and is apparently in good health. Scattered over the arms, legs and trunk are numerous hard elevated intensely pruritic nodules and papules from the size of the head of a brass pin to that of a large pea. The smaller lesions are skin-colored and slightly pigmented and have a smooth surface, the larger ones have a verrucous surface and are a darker brown than the normal skin. There are a few scattered lesions on the scalp. No lesions are present on the mucous membranes. There are no other abnormalities. Palpation and auscultation show the heart, lungs and abdominal viscera to be normal.

The Wassermann reaction of the blood was negative. The sugar content of the blood was 112 mg, the calcium content, 102 mg, and the nonprotein nitrogen content, 36.3 mg per hundred cubic centimeters. Urinalysis showed an acid reaction, a specific gravity of 1.018 and no albumin, sugar or indican. Microscopic examination of the urine showed a few leukocytes and epithelial cells and acid phosphates.

Biopsy of material from large and small nodules showed the following changes: hyperkeratosis, acanthosis, irregular proliferations of rete pegs, large masses of new connective tissue in the corium, most of which had formed around small blood vessels, some hyaline degeneration of collagen and loss of elastic tissue, moderate cellular infiltrations consisting chiefly of lymphocytes, with a few polymorphonuclears, around the vessels, and hyperplasia of the intima of small vessels with partial obliteration of the lumen.

In sections from the normal skin the epidermis appeared normal. In the corium there was some hyaline degeneration of the collagen with formation of new connective tissue. Slight perivascular infiltration with lymphocytes and occasional polymorphonuclears was present.

The cutaneous condition has remained unchanged in spite of treatment, except for transient patches of "eczema" that have appeared on the legs and an occasional papule that appears to become absorbed.

The patient states that six years ago she received injections of sodium iodide, mercury succinimide and neoarsphenamine. The latter drug relieved the pruritus and "weak spells" to which the patient was subject, and it caused some of the spots to disappear. Large doses of calcium and viosterol brought about a lessening of the pruritus, but none of the nodules underwent any change. Freezing the nodules with carbon dioxide snow caused exfoliation of the tops of the lesions but no other change. Thorough desiccation of the nodules caused their temporary disappearance, but they recurred in a few months. Roentgen radiation in doses of from 1 to 3 skin units had no effect on the lesions. Injections of from 0.45 to 0.6 Gm of neoarsphenamine every week or two produced relief from the pruritus and was followed by apparent disappearance of a few lesions.

DISCUSSION

DR WILLIAM H GUY, Pittsburgh. I hesitate to make a suggestion as to investigation in a case of prurigo nodularis on the basis of one observation which my co-workers and I were not able to follow up, but in a case of a similar disorder in the course of the routine physical examination visualization of the gallbladder showed a number of impacted stones. There were no symptoms referable to the biliary tract. I have always wanted to investigate another case

Staining of biopsy material with iodine green disclosed irregular amyloid masses scattered throughout the papillae

The patient has received 2 erythema doses of roentgen radiation in divided dosage, solution of potassium arsenite and yellow mercurous iodide

There have been repeated infections of the leg following excision of material for biopsies, otherwise no change in the condition has occurred

DISCUSSION

DR LOUIS A BRUNSTING, Rochester, Minn Dr Nomland has recently perfected a simple and interesting technic for the demonstration of amyloid in the skin in vivo A small amount of a 1 per cent aqueous solution of congo red is injected subcutaneously in the vicinity of the suspected lesions If amyloid is present it takes up the dye selectively during the next few hours, and the lesions assume a reddish hue, which persists for many days or even months My colleagues and I recently observed a case of systematized amyloidosis in which the zones of amyloid in the skin became stained selectively after the dye was injected intravenously according to the technic of Pautz for estimation of possible visceral involvement

DR R G SENOUR, Cincinnati The congo red stain was tried on this patient's lesions, but there was no retention of the stain

DR HOWARD J PARKHURST, Toledo, Ohio From the clinical standpoint the lesions impressed me as resembling lichen planus ocreaformis. Lieberthal wrote a paper on this subject a number of years ago

DR J EDGAR FISHER, Cleveland About two years ago (ARCH DERMAT & SYPH 26:586 [Sept] 1936) I presented before the Cleveland Dermatological Society a patient with lesions over the extremities, the disorder was diagnosed as lichen planus ocreaformis, and it was quite similar in appearance to that exhibited by this patient The condition is described in Sutton's textbook

DR R G SENOUR, Cincinnati This patient was presented before the Cincinnati Dermatological Society a year ago with a diagnosis of lichen planus ocreaformis of Lieberthal, but when my colleagues and I saw the patient a month ago we called the disorder a mutation to amyloidosis

PSEUDO-ATROPHODERMA COLLI

Miss E K, aged 41, states that her cutaneous disorder began in 1927, the lesions appearing at first as some scaliness about the base of the neck A few months afterward peculiar lattice-work bands were noted This condition seemed to be spreading gradually along the shoulders and down the back and chest No subjective symptoms of any sort have been present The patient is certain that at times the condition seems to be much less obvious than at other times She can assign no reason for this difference Her general health is good Some vague discomfort in the right upper quadrant of the abdomen has been diagnosed as cholecystitis by her attending physician She underwent an appendectomy a few years ago There have been no previous cutaneous disorders

The skin is warm, moist, elastic and exhibits a moderate degree of dermographism The lesions show a diffuse redness and scaliness The involved area seems to be made up of circular depressions covered with bluish-red, linear markings Along the periphery are radiating spots of smooth brownish skin, which at a casual glance resemble the lesions of pityriasis versicolor Tension on the skin seems to obliterate the lesions somewhat

General examination, including examination of the fundi, gave entirely negative results, the blood pressure was 130 systolic and 92 diastolic

Repeated examinations of scrapings of skin for fungi, urinalysis and the Kahn test gave negative results

Biopsy revealed slight thinning of the epidermis, rete plugs and papillae, there was sparse lymphocytic infiltrate scattered throughout the upper portion of the

papules caused their prompt disappearance. Solution of potassium arsenite caused aggravation of the pruritus and increase in the number of papules.

DISCUSSION

DR WINSTON RUTLEDGE, Louisville, Ky. I first saw this patient about three years ago, at that time she presented practically the same picture she now exhibits, except that at varying intervals since then a number of intensely pruritic papules have developed on the trunk and extremities. Histologic examination of one of these papules showed only a dense lymphocytic infiltration in the corium. I treated some of these lesions with roentgen radiation, and some cleared up spontaneously. The histologic studies confirmed the diagnosis of poikiloderma.

DR JAMES M. MARKIN, Rochester, N. Y. I did not notice much atrophy or much telangiectasia in this case. In spite of the history of long duration I think that a diagnosis of mycosis fungoides should be considered. The patient had a pruritic eruption for a number of years, and then this trouble developed. I think that the possibility of parapsoriasis might also be considered. However, in my opinion, the response of the nodules to roentgentherapy and the results of the histologic examination are suggestive of mycosis fungoides.

DR WILLIAM H. GOECKERMAN, Los Angeles. About fifteen years ago I saw a patient with a condition that was rather puzzling, and I looked up the first report that Jacobi made. The condition exhibited by our patient was an exact duplicate of that described by Jacobi. Since then I have been on the lookout for additional cases of the disorder, but I have seen only two. One of these was shown to me by Professor Jadassohn, and the picture was classic. It will be recalled that when he saw Jacobi's case he favored a diagnosis of lupus erythematosus but later rescinded that diagnosis and agreed with Jacobi. I realize that the tendency has always been to include other disorders in the poikiloderma group. For instance, in Chicago in 1933 a number of cases were shown of a rather bizarre eruption classified as poikiloderma, but if one adheres to Jacobi's description I think that one cannot diagnose the condition in any of these cases as poikiloderma. The picture is difficult to describe, but once one has seen a typical manifestation I think it is hard to confuse the condition with anything else. In this case I suggest the diagnosis of pityriasis lichenoides chronica.

DR. H. R. FOERSTER, Milwaukee. The discussion brings up the old controversial question regarding the interpretation of poikiloderma. Do the cutaneous lesions presented by this patient represent a pathologic entity or merely objective symptoms of a transitional stage of some other chronic dermatosis? The atrophic reticulated pigmented lesions presented by this patient suggest to me the clinical picture of the condition known as poikiloderma atrophicum vasculare. The infiltrated, exudative plaques on the back suggest the possibility that this condition belongs to the lymphoblastomatous group, with the picture of poikiloderma making up one phase of the symptomatology and the plaque-like lesions possibly representing beginning tumor formations of the mycosis fungoides type.

AMYLOID DISEASE OF THE SKIN

Mr. J. B., aged 50, states that lesions appeared on the legs in the early part of 1933, after an infection of the upper portion of the respiratory tract. No lesions were present elsewhere on the body. No history of any previous cutaneous lesions of any sort could be elicited.

Physical examination gave essentially negative results.

Both legs are covered with hypertrophic polygonal brownish-red papules, the eruption being most marked on the anterior aspect. The upper extremities are not affected, the mouth shows no abnormalities.

The Kahn test and urinalysis gave negative results. The cholesterol content of the blood was 133 mg per hundred cubic centimeters. The congo red test gave normal results.

ticularly struck by the dense fibrous tissue and the very large lymphatic spaces. Cutting into some of these lymphatics was like cutting into small serous cysts. Below the knee the fascia was removed from the midline anteriorly to the midline posteriorly and a great deal of scarred subcutaneous tissue and fat, along with it. The scarring down over the lymphatics was not nearly so prominent above the knee as below. During the operation, some of the tissues were taken for culture. Bleeding points were ligated with silk and the wound closed with interrupted medium silk sutures throughout without drainage."

This operation gave the patient slight relief, but even after this the acute episodes continued. He also showed evidence of pituitary dyscrasia with possibly Frohlich's syndrome. Roentgenograms of the legs showed a considerable network of shadows. The bones remained normal.

There is a fairly definite history as far back as the grandfather, who had swollen legs. The grandfather married twice, his first wife bore two daughters. One died in infancy, of unknown cause, in the second, edema of the legs developed at puberty. Her children, two girls, were likewise affected with edema of the legs at puberty. By his second marriage several children were born, but information was obtained about only two of them. Both were males and had swelling of the legs, which began at about the fourteenth year. One, the father of the patient, has been married twice. By his first wife two children were born, these remained normal, one is 30 and the other 35 years of age. By his second wife two children were born, the patient and his brother. Both have edema of the legs. The father of the patient has had acute attacks, first at the age of 14, consisting of swelling in the right groin associated with malaise, chills and fever. He has exhibited swelling of the entire right leg, redness, tenderness and pain, followed after several days by increase in the size of the legs and desquamation. He has had a hundred or more of these attacks. A half-sister of the patient's father has had more frequent and more severe attacks.

The patient's heart and lungs are normal. The visual fields are normal.

The condition is limited to the lower extremities. There is enormous edema of the ankle and leg between the knee and the ankle. The edema is semisolid, cool and nontender. Measurements at one time were as follows: right ankle, 35 inches (88.9 cm), right calf, 44 inches (111.76 cm), left ankle, 34 inches (86.36 cm), left calf, 46 inches (116.84 cm). After rest in bed for four days, the right ankle measured 30 inches (76.21 cm), the left ankle, 33 inches (83.82 cm), the right calf, 40 inches (101.6 cm), and the left calf, 45 inches (114.3 cm).

The basal metabolic rate ranged from -15 to -20 per cent. The Wassermann test was negative. Chemical examination of the blood showed 11 mg of urea nitrogen, 65 mg of sugar, and 427 mg of chlorides, per hundred cubic centimeters. The dextrose tolerance test and urinalysis gave negative results. The blood count showed 5,240,000 erythrocytes, 7,600 leukocytes and 75 per cent hemoglobin. The results of the differential count were as follows: polymorphonuclears, 67 per cent, lymphocytes, 30 per cent, large mononuclears, 2 per cent, eosinophils, 1 per cent. Cultures of the blood gave negative results on several occasions. Cultures of tissue by Dr. McGuire showed hemolytic streptococci.

The mucous membrane is clear.

The febrile episodes continue to appear at somewhat less frequent intervals.

Treatment has consisted of administration of streptococcus vaccine and, later, of administration of antiserum (Foshay).

DISCUSSION

DR. LESTER HOLLANDER, Pittsburgh. The interesting thing is the dystrophia adiposogenitalis which the boy presents. The genitals are very small. I have observed a case of Milroy's disease in a boy aged about 10 years, in which a similar syndrome occurred. I do not know whether one is justified in calling the disorder a Frohlich syndrome, but think that abnormality is of importance in conjunction with the other findings.

corum, the Verhoeff eosin, Van Gieson and Foot-Foot stains showed no disturbances of the collagenous and elastic tissue

The patient received treatment for a few months, but no appreciable change in the appearance of the lesions resulted. In August 1935 the lesions were definitely improved, at that time the patient was receiving no treatment of any sort. The area has not been exposed to the sun.

Treatment has consisted of local massage and administration of thyroid gland preparations.

DISCUSSION

DR S W BECKER, Chicago. This patient's condition corresponds in every detail to that which Dr Muir and I described (*ARCH DERMAT & SYPH* 29 53 [Jan] 1934) under the name of pseudo-atrophoderma colli. This patient's lesions are more extensive and more evident than any I have seen. There are evidently slight epidermal atrophy and a loss of elasticity, which account for the smoothness of some of the plaques and the cigaret-paper crinkling between the smooth plaques. One case which I observed many years ago in Dr O'Leary's service at the Mayo Clinic was reported by Dr Jeffrey Michael, who stated that complete restoration to normal occurred after many years, this makes me believe that there is no real dermal atrophy in this condition.

DR ELMORE B TAUBER, Cincinnati. In this case, as in that which Dr Becker and Dr Muir reported, the lesions are generally worse in winter, in fact there have been periods in the summer when there was no atrophy or shininess and the skin looked practically normal.

DR RICHARD S WEISS, St Louis. I suggest that the diagnosis of pseudoxanthoma elasticum be considered in this case.

DR JACK JONES, Atlanta, Ga. When I examined this patient the light was not very good, but I tried to find the features of pseudoxanthoma elasticum. She states that she had a definite ocular disturbance. My colleagues and I have seen twelve or fifteen cases of pseudoxanthoma elasticum associated with angioid streaks of the retina, and I wonder whether in this case angioid streaks are not present also.

DR ISADORE ROSEN, New York. Dr Tauber said that in the summer the lesions disappear. I cannot understand how areas of skin affected by dermatosis with atrophy can regenerate. I suggest the diagnosis of tinea versicolor, and I think that repeated examinations should be made for *Microsporon furfur* because one occasionally sees patients with this infection whose lesions clinically give the appearance of atrophy.

DR HOWARD J PARKHURST, Toledo, Ohio. Many of these lesions show follicular plugs, and I think that the diagnosis of lichen planus atrophicus should be considered.

A CASE FOR DIAGNOSIS

Mrs G G, aged 26, has been presented at various dermatological conventions throughout the country in the past five or six years, exhibiting some of the various phases of her condition. No definite diagnosis has been made. The cutaneous lesions appeared approximately one year after birth. The picture has varied from that of dermatitis exfoliativa to that of a skin almost normal except for discrete scaling erythematous patches. Occasionally the patient complains of subjective symptoms of pruritus and burning, but there are no other disturbances.

There is no family history of psoriasis. Physical examination gave essentially negative results. Few discrete areas are visible at the present time.

The Wassermann test, urinalysis, determination of the sugar and urea content of the blood and blood counts gave normal results. No eosinophilia was present on repeated smears.

One biopsy was reported by Dr Goeckerman to show psoriasis.

has varied somewhat. My colleagues and I decided to present this patient because we believed that she exhibits good examples of the three types of lesions that are described in cases of circumscribed myxedema, namely, the diffuse thickening of the skin, the localized nodular thickenings and the keloid-like papules. We were not certain whether the lesions were keloids, therefore an additional biopsy was made, which revealed myxedema.

DR LOUIS A. BRUNSTING, Rochester, Minn. This plaque shows the typical features of so-called circumscribed myxedema. Occurring, as is usually the case, in association with hyperthyroidism, it represents an unusual physiologic paradox. The lesions occur on the lower portion of the legs, almost without exception, this may possibly be explained on the basis of circulatory stasis gradually interfering with the supply of thyroid hormone to these parts.

KRAUROSIS VULVAE

B. T., a woman aged 51, has complained of some pruritus of the genitalia for the past five years, but recently the condition has become considerably aggravated. No therapy, except local applications of various ointments and lotions, has been used. The patient has received treatment for latent syphilis for the past two years. No details were available concerning her syphilitic infection. A panhysterectomy was performed in 1915.

There is no family history of syphilis, tuberculosis or malignant disease. Some mental insufficiency is noticeable, but otherwise there are no abnormalities. No leukoplakia buccalis is present. There is almost complete obliteration of the labia pudendi. The skin is thickened. Vaginal inspection shows no abnormalities.

The Kahn test was positive. Urinalysis gave negative results until recently, when inconstant glycosuria was found for the first time. A dextrose tolerance test showed diminished tolerance.

Histologic examination of a section showed atrophy of the epithelium, few papillae were seen, rare areas of the epidermis, at one edge of the section, showed vacuolation and some irregular grouping of prickle cells, few mitoses were also present in these areas, there was lymphocytic infiltration in the derma, some increase in fibrous tissue and a few glandular appendages were also observed.

Treatment has consisted of local application of soothing preparations and of injections of pituitary extract and ovarian extract. The diabetes is controlled at present with dietary restrictions.

DISCUSSION

DR LESTER HOLLANDER, Pittsburgh. The treatment of kraurosis vulvae should consist of complete and radical vulvectomy, and this should be done early. Dermatologists should not temporize with roentgen therapy or other forms of treatment because delay may be serious as these lesions are potentially malignant.

DR EARL D. OSBORNE, Buffalo. I agree with Dr. Hollander regarding vulvectomy in cases of true kraurosis vulvae. I believe, however, that section of the pubic and long pudendal nerves is also essential for permanent results. I believe that it is the practice at the Mayo Clinic to sever those nerves. My colleagues and I have had three patients who were treated in that manner, and splendid results were obtained.

DR MARION B. SULZBERGER, New York. I was interested in this case particularly because of the lack of leukoplakia. It is a case of kraurosis associated with latent syphilis but without leukoplakia.

I wonder whether any of the members have had any experience with theelin therapy in cases of pruritus vulvae. It is known that this hormone has a marked effect on the vulvar epithelium, demonstrable in infants and young children. It increases the cornification. I have treated one patient with intractable pruritus vulvae with injections of theelin and have obtained apparently excellent results. The pruritus stopped, after many years' duration, and without other therapy.

DR LOUIS A. BRUNSTING, Rochester, Minn. This type of true kraurosis vulvae, with or without leukoplakia, should be distinguished from the more com-

lips and nose. The biopsy specimen was typical of psoriasis. Her pregnancy apparently had no effect on the appearance of the lesions. I recall definitely that neither ultraviolet irradiation nor local applications had any effect on the lesions.

ICHTHYOSIS HYSTRIX

H. H., a boy aged 13, has had the present cutaneous condition since birth. There is marked dryness of the skin, and it is scaly, so-called "fish skin." Ulcers frequently develop on the hands or feet.

The patient's father has pulmonary tuberculosis. Except for that, the family history is irrelevant.

The skin shows generalized thickening, and there is a marked desquamation, giving a fish-scale appearance. Superficial ulcers are present on both wrists, knees and ankles and on the abdomen.

Physical examination gave essentially negative results except for a purulent discharge in the left ear. The tonsils were hypertrophied and inflamed. There was serous discharge from the nose.

The Wassermann test and urinalysis gave negative results. Examination of the blood showed 4,500,000 erythrocytes and 11,000 leukocytes. The differential count gave the following results: polymorphonuclears, 68 per cent, lymphocytes, 25 per cent, mononuclears, 5 per cent, and transitionals, 2 per cent. The basal metabolic rate averaged $+4$ per cent on three different tests.

Biopsy revealed marked hyperkeratosis and occasional areas of parakeratosis, pyknosis and vacuolation of basal cells and a decrease in the number of prickle cells, lymphocytic and polymorphonuclear infiltration, a sparsity of blood vessels, a few of the vessels present being dilated, and some increase in collagenous tissue.

The condition is the same as it was when the patient was admitted to the hospital.

No treatment has been given.

DISCUSSION

DR RICHARD S. WEISS, St. Louis. I suggest a diagnosis of congenital ichthyosiform erythroderma. The patient has a reddened skin and ichthyotic patches. The ichthyotic manifestations are not thickest on the sites where ichthyosis ordinarily occurs, namely, the extensor surfaces of the forearms, arms, legs and thighs, on the contrary, they are thickest about the joints, particularly about the elbows and knees, and there are lesions about the axillary folds and the buttocks. The condition is, I think, the dry form of congenital ichthyosiform erythroderma. In addition, the patient exhibits the dry scaly scalp so often associated with this disease.

DR HOWARD J. PARKHURST, Toledo, Ohio. I think that the disorder is congenital ichthyosiform erythroderma with formation of bullae. The crusted lesions are suggestive of that condition.

MILROY'S DISEASE.

(This case was reported by Dr. McGuire and Dr. Zeek in *The Journal of the American Medical Association* (98:870 [March 12] 1932).)

Mr. M. W., aged 21, in 1926 first noticed swelling of his legs, not associated with a systemic reaction. Recently, however, he has been repeatedly hospitalized because of febrile episodes. In 1930 the Kondoleon operation was performed by Dr. Reid, the procedure being described as follows: "Incision was made from just below the greater trochanter down to the external malleolus. In the thigh about one-half inch of skin was removed and below the knee a little less than this amount. After getting through the skin and little subcutaneous tissue the flaps were widely undermined, both above and below the knee. This was carried to a point beyond which we were afraid that circulation to the edges of the flap would be impaired. A large amount of the subcutaneous fat and fascia and the fascia of the muscles were removed from above and below the knee. Below the knee one was par-

DR. I J ARNSSON, Buffalo I wish to call attention to an article which Weidman and White wrote some years ago on the technic of sectioning material for biopsies. If the sections are cut the wrong way one may get pictures which are similar to those of so-called malignant conditions. It is always advisable to examine the sections under high magnification. In true malignant degeneration such as squamous cell carcinoma one would not see islands with basal cells around them, but in the case under consideration one cannot demonstrate a single section without a border of basal cells.

DR MAX SCHEER, New York It is possible to mistake the excessive acanthosis of the margin of an ulcer for basal cell epithelioma. But in this case the inguinal gland showed squamous cell carcinoma.

EPIDERMOLYSIS BULLOSA

This boy, aged 2 years, has an eruption which has been present since birth. There is no family history of any type of cutaneous disease. The mother and father are living and well.

Physical examination gave essentially negative results. The skin presents all the classic lesions of the disease.

The results of laboratory examination were negative.

Biopsy showed extensive separation of epithelial layers with formation of vesicles, there was some lymphocytic infiltration in the corium, no staining for elastic tissue was done.

Bullae continue to develop at points of trauma, especially on the hands and feet.

DISCUSSION

DR RICHARD S WEISS, St Louis I wish to ask whether the presenter made studies of the apparently normal skin for loss of elastic tissue. Many of the members may recall that Engman and Mook and also Kanoky and Sutton reported diminution and fragmentation of the elastic tissue of the apparently normal skin of patients with epidermolysis bullosa. I subsequently was able to confirm these observations.

DR ELMORE B TAUBER, Cincinnati Such an examination was not made. The sections did show loss of elastic tissue, but no biopsy of the normal skin was made. The only thing I thought remarkable in this case was the response to the therapy used. The normal oil of the skin containing stearin was used, and in addition ultraviolet radiation, extract from the anterior lobe of the pituitary and small doses of thyroid extract were given. Originally by rubbing, a bulla could be produced at any time, but the members may have noticed that rubbing the patient's soles or body today did not produce the same response. The child is only 2 years old and, of course, one does not know what will happen.

DR LESTER HOLLANDER, Pittsburgh I do not wish to discourage Dr Tauber about his treatment, which is excellent, but I wonder whether the same result would not have occurred without treatment. I think that these disorders improve as the patients grow older.

DR WILLIAM H GUY, Pittsburgh My opinion is that epidermolysis bullosa has some connection with glandular disturbances. In many children the disorder clears up or improves at puberty. When the condition develops after puberty it does not respond to any therapy. Recently Beinhauer has tried treatment by injections of theelin and has reported clearing of the lesions. My co-workers and I have tried that method of treatment in two cases without effect. I believe that the administration of estrogenic hormone should be given a trial in the early phases of the disease.

EPIDERMOLYSIS BULLOSA, FORME FRUSTE

Miss F S, white, aged 20, has a congenital abnormality of the finger-nails and toe-nail, which has been present since birth. There were no cutaneous lesions until 1930, when painful blisters, large and small, began to appear spontaneously.

DR R A C WOLLENBERG, Detroit As I understand Milroy's disease, it is quite distinct from the condition exhibited by this patient I consider his disorder to be sporadic elephantiasis due to obstruction of the lymph vessels, with hypertrophy and edema, resulting from infection about the feet and toe-nails Whether this condition is a fungous infection or one due to pyogenic organisms, it is quite distinct from Milroy's disease In cases of the latter condition there is enlargement or hypertrophy of the legs without blocking of the lymphatics It is a chronic hereditary disease and is probably of a trophic nature

In this case focal infection could probably be eliminated by removal of the toe-nails

DR. LEON GOLDMAN, Cincinnati This patient had elephantiasis, which appeared when he was about 12 Several years later the episodes of cellulitis began to develop The condition occurs in his family My colleagues and I have tried repeatedly to find some cause for the cellulitis and the lymphangitis Cultures of tissue have been made under various conditions The sections of skin have been examined repeatedly for organisms, but none has been found We intend to give the patient some streptococcus vaccine We have asked the surgeons repeatedly to remove the toe-nails, but they think it inadvisable to do so before the infections subside for an appreciable length of time

DR FRED WISE, New York I am curious to know whether there is any abnormality of the testicles, or anything suggesting Frohlich's syndrome I think this is an important point in the diagnosis

DR MARION B SULZBERGER, New York I agree with Dr Wollenberg, and I wish to state that Dr Williams and Dr Traub in New York have recently investigated cases of recurrent erysipelas-like lesions of the legs and feet I had an opportunity to see one patient and to study the disorder That patient was tested with trichophytin applied by the usual method on the arm and intracutaneously The reaction was negative after twenty-four and forty-eight hours However, on the skin of the affected leg, proximal to the affected area, there was a strongly positive immediate reaction in the form of a wheal There was also a high titer of passive transference antibodies to trichophytin in that patient's serum Dr Williams, Dr Traub and I regarded that disorder as being due to a localized lymphatic or vascular immediate wheal type of sensitivity to fungi, and not erysipelas

DR LESTER HOLLANDER, Pittsburgh I have studied a case of a similar disorder in which the same picture appeared on the dorsum of the foot

DR LEON GOLDMAN, Cincinnati As to Frohlich's syndrome, there is a typical clinical picture of that in this case, but all laboratory evidence is negative He has received no treatment with pituitary extract My co-workers and I still hold to the clinical diagnosis of Milroy's disease

LOCALIZED MYXEDEMA OF THE SKIN

A P, a Negress aged 32, has an irrelevant personal and family history
Serologic tests and urinalysis gave negative results
Biopsy revealed the typical picture of myxedema

Little clinical change has resulted from the administration of thyroid extract, although the patient states that her legs felt better while she was receiving that medication

Thyroid extract has been used as indicated, no local treatment has been employed

DISCUSSION

DR MAX SCHFER, New York It seems curious that in a certain proportion of these cases the patient is likely to show hyperthyroidism rather than hypothyroidism That may be one reason for the lack of therapeutic response to thyroid What do the determinations of basal metabolic rate show?

DR. A B LOVEMAN, Louisville Determinations of the basal metabolic rate were made and the rate was over normal before operation After operation it

The Wassermann reaction was negative. Examination of the urine showed albumin (1 plus). The blood count showed 4,700,000 erythrocytes and 19,300 leukocytes, the hemoglobin content was 10.5 Gm per hundred cubic centimeters. The results of the differential count were as follows: polymorphonuclears, 62 per cent, eosinophils, 6 per cent, lymphocytes, 25 per cent, large mononuclears and transitionals, 7 per cent. Tests with tuberculin gave negative results. Culture of material from bullae gave negative results on several occasions, then *Streptococcus viridans* and *Oidium albicans* were obtained.

Biopsy showed irregular separation of epithelial layers, no definite bullae were seen, there was scattered polymorphonuclear and lymphocytic infiltration in the corium, with some perivascular distribution, no staining for elastic tissue was done.

There has been improvement, especially of the lesions in the mouth.

Treatment has consisted of administration of viosterol, of a preparation of carotene and of brewers' yeast, local treatment with neoarsphenamine, and generalized treatment with sodium thiosulfate.

DISCUSSION

DR. TOULMIN GAINES, Mobile, Ala. In these three cases there is no family history of consanguinity.

DR. LESTER HOLLANDER, Pittsburgh, Pa. I wish to call attention to the treatment in this case, namely, administration of viosterol, of a preparation of carotene and of brewers' yeast, local treatment with neoarsphenamine, and generalized treatment with sodium thiosulfate, as compared with the treatment in the previous case, in which excellent results were likewise obtained.

DR. R. G. SENOUR, Cincinnati. I saw this patient at the Children's Hospital about three weeks ago, and all this therapy had been used before that time.

DR. RICHARD S. WEISS, St. Louis. This patient's condition interests me because of the fact that my colleagues and I have a patient with a like disorder at the Children's Hospital in St. Louis. Because we could not come to any definite conclusion we diagnosed the condition as epidermolysis bullosa with a question mark, and the question mark is still there. In that case the lesions tended to disappear at certain seasons and recurred. Was a like variation noted in this case?

DR. R. G. SENOUR, Cincinnati. According to the history there is no seasonal variation in this case.

DR. FRANK W. CREGOR, Indianapolis. I believe that the reticulo-endothelial system supplies the means whereby the epidermis is held fast to the derma and that a defect in that system accounts for the development of the syndrome called epidermolysis bullosa hereditaria.

I believe that changes in the body structure which result from hormones coming into the circulation at puberty account for the improvement observed in cases of this disorder at that time.

ACUTE LUPUS ERYTHEMATOSUS (RECOVERY)

L. V., a woman aged 26, was first seen on May 16, 1935, she had a cutaneous disorder of three weeks' duration, which began as small reddish blotches. There was no pruritus. The patient was sent to the hospital on May 27.

There are no physical abnormalities. When the patient was first seen she had six discrete maculopapular lesions on the side of the nose, face and forehead, which were slightly scaly and slightly burning, within nine days the lesions coalesced, forming a typical bat wing, slightly elevated lesion involving the nose and cheeks symmetrically. The temperature is 99.8 F. One erythematous lesion is present in the center of the hard palate. Lesions which appeared later are present on the extensor surfaces of the arms.

Examination of the blood on May 20 gave normal results. The urine was normal until serum sickness developed. Daily blood counts showed leukopenia.

mon neurodermatitis of the vulva with lichenification in cases of which subjective symptoms of pruritus are more prominent. Because of the prospect of ultimate malignant degeneration in this case the treatment of choice is surgical resection of the vulva. Whether the pudendal nerves should be resected is dependent on the degree of symptomatic discomfort that exists in any given case.

DR FRANK W. CREGOR, Indianapolis. I wonder what effort has been made to demonstrate a fungus in this case. In my opinion the disorder lacks many of the features of kraurosis.

I had the nurse remove the patient's slippers and I found a mycotic infection between the toes of both feet. I think that careful examination should be made before subjecting the patient to a vulvectomy.

DR H. L. CLAASSEN, Cincinnati. My co-workers and I have found no evidence of any fungous infection.

SQUAMOUS CELL CARCINOMA OF THE RIGHT FOOT WITH INGUINAL METASTASES

Mr. E. K., aged 62, says that this condition began in 1932 with a "callus" on the sole of the right foot. He operated a power machine and believed that this "callus" followed continued operation with the right foot. In January 1934 he first complained of soreness, and at that time the "callus" seemed to become rougher and larger. He consulted a physician, who gave him some form of chemical cauterization and special shoes, but this produced no relief. The lesion continued to grow and became more painful. He was admitted to the hospital in January 1935. There is no family history of malignant disease of any sort.

Photographs showing the progress of the lesion from a large fungating papillomatous mass to the present ulcer are presented. Firm glands in the right inguinal area were noted only four months ago.

The Kahn reaction and urinalysis were negative. Roentgenograms of the metatarsus gave negative results. There was some rarefaction in the distal phalanx of the right big toe.

Biopsies have been made at intervals and showed early development of squamous cell carcinoma. Biopsy of material from the inguinal gland also showed squamous cell carcinoma.

In the early part of March 1935 complete electro-excision and electrocoagulation were employed. These procedures were followed shortly afterward by roentgen therapy, a total of 2,712 roentgens of unfiltered radiation being administered. The patient is receiving roentgen radiation to the inguinal glands.

DISCUSSION

DR I. J. ARNSSON, Buffalo. I suggest a diagnosis of ulcer following surgical removal of a benign papilloma. All the slides presented failed to show malignant degeneration, and the so-called metastases in the lymph gland failed to show any squamous cells. The so-called islands of epithelial cells were surrounded with basal cells.

DR ELMORE B. TAUBER, Cincinnati. This patient originally exhibited what I thought was papilloma of the foot, there was a great deal of secondary involvement. I insisted on that diagnosis, but gradually because of the great weight of opinion and of the biopsy report I reluctantly relinquished my diagnosis. I am glad that Dr. Arnsson brought out that point, for that was my original diagnosis.

DR H. JERRY LAVENDER, Cincinnati. At least half a dozen sections were sent to different pathologists in various places and the consensus was that the condition was squamous cell carcinoma.

DR A. B. LOVEMAN, Louisville, Ky. It should be emphasized that occasionally good general pathologists report the presence of carcinoma in material which undoubtedly exhibits examples of pseudo-epitheliomatous hyperplasia. This occurred recently on two occasions of which I am aware. One section was taken from the edge of an ulcer and the other from a hypertrophic growth on the vulva of a patient with lymphogranuloma inguinale.

now has no lesions except residual patches consisting of slight atrophy and roughness of the affected areas with a scarcely discernible border. It is now five months since she was discharged from the hospital.

My colleagues and I considered this case worth presenting because of the therapy used, and we hoped that it might prompt others to use antistreptococcus serum in similar cases.

DR S W BECKER, Chicago. I wish to call attention to the fact that vaccine or serum therapy must be used with great caution. My co-workers and I had one patient who had received vaccines. We treated her with quinine orally, but she became worse and died in a few weeks. In another case a surgeon had made a diagnosis of erysipelas and given antierysipelas vaccine, and the patient became acutely ill after receiving the treatment. Patients with this condition are highly sensitive to vaccine or serum of any kind, and it must be used with great caution.

DR DANIEL J KINDEL, Cincinnati. I cannot subscribe to the opinion that our treatment was too drastic, for this disease is so uniformly fatal that I do not see how much, if anything, is to be lost by proceeding with serum therapy properly controlled. In this case we had the advantage of consultation with Dr Lee Foshay, an expert on serum therapy, who provided us with the material.

NOTE.—The patient is well at present and the skin is clear.

LUPUS ERYTHEMATOSUS

Mr F R, aged 37, states that lesions appeared on his face in 1925, after he sustained a burn. There are no subjective symptoms and no known familial history of pulmonary, glandular or osseous tuberculosis, rheumatic fever, heart trouble or syphilis.

Physical examination gave negative results. On admission to the clinic in 1929 there were typical butterfly lesions over the face and along the sides of the neck. The hands were clear.

The results of the Wassermann test and urinalysis were repeatedly negative. No biopsy was made.

This patient is presented chiefly because of the therapeutic aspect of the case. He received 5.5 Gm of neoarsphenamine from June 28, 1929, to Jan 30, 1930. From Oct 11, 1929, to the present time he has received gold and sodium thiosulfate. The first few doses consisted of 0.1 Gm, then 0.3 Gm was given regularly. One hundred and eighteen injections were given, and the total amount of gold and sodium thiosulfate administered was 32.5 Gm. Periods of rest, averaging one month, were given every five to six months. No local or systemic reactions were noted. Considerable scarring remains.

DISCUSSION

DR RICHARD S WEISS, St Louis. I was much impressed with the therapeutic result in this case, but when I read that 32.5 Gm of gold and sodium thiosulfate was administered in a period of six years I was astonished. That seems to be a terrific amount. My co-workers and I are becoming more and more cautious the more treatment with gold compounds we use and the more we observe its effect on the leukocyte count. I wish to issue a warning that patients who receive gold preparations must be carefully watched, often excellent results can be obtained with a minimum amount of a gold preparation.

DR ELMORE B TAUBER, Cincinnati. When Dr Wright read his paper last May I reported this case and stated that it was the exception which proved the rule.

DR R G SENOUR, Cincinnati. I have treated this patient with a gold preparation for five years, and at the last meeting he had received 7.5 Gm. I was then warned. I watched him carefully. He has received 32.5 Gm of gold and sodium thiosulfate all together. I think this patient shows real tolerance for the drug.

over the feet. They seemed to respond slightly, but not entirely, to local application of various ointments. The skin in general is somewhat dry, and there is a mild acne of the face. There is no family history of a similar condition or of syphilis or tuberculosis.

General examination gave essentially negative results. The nail of the left large toe was removed surgically about three years ago, otherwise the nails show no changes. Spontaneous bullae appear on the normal skin chiefly at the base of the toes on the dorsa of the feet. The large oozing areas on the soles dry at times, heal with great difficulty and shortly afterward break down again.

Scrapings and culture were negative for fungi.

The patient has been under observation for a year and a half. The bullae which appeared spontaneously at the base of the toes have healed at times. The large areas on the feet seem to dry up considerably after roentgen therapy, but a relapse soon occurs.

The patient has received 1 erythema dose of roentgen radiation in divided doses. Local therapy has consisted chiefly of baths of potassium permanganate and application of calcium chlorate ointments.

DISCUSSION

DR S S GREENBAUM, Philadelphia. In addition to the thickened nails, this patient has an oral abnormality. The lateral borders of the tongue show a thickened whitish condition which resembles leukoplakia. I think that the condition belongs in the group described by Jadassohn under the name *pachyonychia congenita*. A case somewhat similar to this one was described recently by Cole, Rauschkolb and Toomey.

DR HOWARD J PARKHURST, Toledo, Ohio. Why was roentgen therapy used in this case?

DR FRED WISE, New York. I think the disorder presents most of the features of *pachyonychia congenita* described by Jadassohn, and I do not think that it is *epidermolysis bullosa*.

DR WILLIAM H GUY, Pittsburgh. I had great difficulty in agreeing with the diagnosis of *epidermolysis bullosa*, and I am pleased to hear Dr Wise's remark. I wish he would elaborate on the changes in the skin which simulate *epidermolysis bullosa* and on the method of development. Does he believe that these cutaneous lesions have the same etiologic background as the changes in the nails?

DR FRED WISE, New York. In the few cases of *pachyonychia congenita* associated with dermatitis and hyperkeratotic lesions which I have seen there were also changes in the nails and on the tongue. I think there is an artefact in this patient. The patient was treated and removed the top layer of skin, this produced a lesion like one of *epidermolysis bullosa*. The spaces between the toes presented areas like eczema in the few cases of this condition which I have seen.

DR ISADORE ROSEN, New York. I wish to make one or two other suggestions in regard to this case. In view of the repeatedly negative results of examinations for fungi, I think one should consider the possibility of pustular psoriasis or *acrodermatitis continua* of Hallopeau.

EPIDERMOLYSIS BULLOSA (?)

This child, aged 2 years, has lesions which appeared at 3 months of age and consisted of vesicles and bullae distributed over the head, face, arms, legs, toes and fingers. When the patient was 1 year of age, severe ulcerative stomatitis associated with the cutaneous lesions developed. No similar disorders are known to have occurred in the family.

Bullae are present on the extremities, and there is atrophy at the site of former lesions.

Physical examination showed no essential findings other than malnutrition.

should be made. This case emphasizes again the importance of watching for cutaneous manifestations associated with this venereal entity. It has been my experience and that of my co-workers in about two hundred and fifty cases of lymphogranuloma inguinale that in certain cases, aside from the glandular picture, there are outbreaks of purpura, erythema nodosum and generalized papulopustular lesions, which, in certain respects, simulated a papulonecrotic tuberculid.

DR H L BAER, Pittsburgh. Apropos of tularemia, I think that the history in this case is confusing. Tularemia is one disease in the presence of which the cutaneous test and also the agglutination tests may remain positive for a period of almost twenty years. I think that the negative results of the tests would exclude the possibility of tularemia in this case.

DR HOWARD HAILEY, Atlanta, Ga. I agree with Dr Sulzberger and Dr Goeckerman that the condition of the skin is due to a pyogenic infection. The draining sinuses in the axilla, I believe, are likewise due to a pyogenic infection. Thorough curettage of the sinuses should bring about a speedy recovery. I have seen this clinical picture in the axilla several times previously. It usually occurs in patients with acne vulgaris, and this patient presents scattered lesions of acne.

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NOTE—A Frei test was made and gave negative results.

ATOPIC ECZEMA, CONGENITAL SYPHILIS

R J, a Negro boy aged 3 years, was first admitted to the hospital on Feb 15, 1935, and has been in the hospital since then. The condition appeared on the face five months before admission and then spread gradually to the scalp and extremities. The patient was born at full term, and delivery was normal. No details of the infant feeding are known. He had no illnesses of any sort before admission.

There is no known family history of allergy, tuberculosis or syphilis. Two other children in the family have no cutaneous diseases.

Physical examination gave negative results except for a persistent nasal discharge. No viscera were palpable in the abdomen.

On admission the patient had considerable oozing and edema of the entire face and scalp, associated with a generalized papular eruption.

The Kahn test was positive. Examination of the urine, a blood count and roentgen examination of the chest disclosed no abnormalities. Tests with human and bovine tuberculin and with all food and inhalant antigens gave negative results. Cultures suggestive of the Klebs-Löffler bacillus were obtained at times from the nose, virulence tests, however, gave negative results. Scrapings from the scalp showed no fungi.

Fever therapy was administered and the patient has since had no extensive oozing of the face. Papular eruptions still occur frequently. After a 100 per cent preparation of crude coal tar was applied a few months ago there developed increased swelling of the face, associated with drowsiness, oliguria and hematuria. No reactions followed application of 2 and 5 per cent coal tar ointments.

Treatment has consisted of elimination diets, including cod liver oil and calcium, courses of acetarsone, and administration of linseed oil. The Kettering hypertherm has been used, protective coverings have been applied to the patient's pillows and mattress. The patient has received local therapy to the nose, daily tar baths and local applications, chiefly of tar preparations.

DISCUSSION

DR R G SENOUR, Cincinnati. I should like to have some therapeutic suggestions.

DR MARION B SULZBERGER, New York. I should like some suggestions as to the diagnosis. I can see no reason for calling this disorder atopic eczema. There

Roentgen examination of the chest gave negative results. Culture of the blood gave negative results on two occasions while the patient was in the hospital, the sedimentation rate was decidedly increased.

No biopsy has been made.

The patient had a slight elevation of temperature and became progressively worse after admission to the hospital. The intensity of the eruption increased.

She was given 180 cc of antistreptococcus serum (prepared by Foshay) intravenously, 60 cc being given daily for three days. There followed severe and prolonged serum sickness, lasting fifteen days, with massive enlargement of lymph glands and marked and continuous urticaria associated with purpura and severe pains in the joints. The eruption began to fade after the second week, leaving some brownish pigmentation and slight scaliness. The patient left the hospital in three weeks, and the outline of the eruption could be plainly seen for two or three months.

DISCUSSION

DR RICHARD S. WEISS, St. Louis: This case is labeled one of "acute lupus erythematosus (recovery)." I do not think that recovery has occurred. The patient presents a type of lupus which my co-workers and I have been recognizing for quite a while and to which Dr. M. F. Engman, Sr. has called our attention on numerous occasions. In this type of condition there is a faint erythematous, slightly scaling eruption at first limited to the face and with only a suggestion of atrophy. It usually occurs in women aged between 17 and 30, especially in those who are under a severe social strain and who are living an active life. The cases of this disorder which we have observed have led us to believe that this particular type of lupus erythematosus is often the precursor of the acute exanthematic lupus erythematosus, I regard the prognosis in this case as grave, especially as the patient has leukopenia.

DR DANIEL J. KINDEL, Cincinnati: In one way I am glad to hear Dr. Weiss say that this patient still has lupus erythematosus disseminatus, because there seems to be some question as to whether she has had that disease, and the residual markings can scarcely be detected. One must recognize that in the management and therapy of the acute disseminated form of lupus one is grasping at straws for a solution. In most cases the condition terminates fatally.

Three months before this patient was first seen, my co-workers and I treated a boy, aged 15, who after three weeks' hospitalization and a stormy course died of lupus erythematosus disseminatus. He was toxic, and the disease was far advanced when we first saw him. Culture of the blood on two occasions shortly after admission gave negative results. The boy did not receive the serum which we used in this case. He died as the result of an invasion by hemolytic streptococci, and autopsy showed all the cavities of the body filled with a brick-red fluid. I am aware of the fact that some observers consider septicemia in these cases as a secondary or terminal invasion. The organism was recovered and a vaccine prepared for possible subsequent use.

The woman who is presented also had a negative blood culture on admission to the hospital, but in view of our recent experience we decided to administer a specially prepared and potent antistreptococcus serum, prepared by Dr. Lee Foshay of the bacteriology department of the University of Cincinnati. The woman was tested with the vaccine for sensitization to the streptococcus recovered from the boy and showed a slight but positive reaction. One hundred and eighty cubic centimeters of serum was given intravenously within three days, 30 cc of serum being injected morning and evening. Within a week there developed a severe serum sickness, lasting for fifteen days, with marked generalized lymphadenopathy involving even the nodes of the scalp. There were marked headache, arthritic pains, petechial hemorrhages in the skin and gastro-intestinal disturbances. Until shortly before the termination of the serum sickness the lesions on the face and arms persisted, later they faded gradually. When the patient left the hospital the lesions were still noticeable, but very faint. She continued to improve at home, and she

middle-aged member of the dermatologic group, I still find it difficult. The main difficulty is that as far as immunologic therapy is concerned the results in my experience are nil. As far as my co-workers and I have been able to carry out cutaneous tests and to check these by elimination and by renewed exposures to the substances eliciting positive cutaneous reactions, we have been unable to prove that many of those substances influenced the course of the dermatosis. After all investigations of this type we have to return to the old topical therapy. However, I must state that I, for one, have never been able to carry out the elimination and renewed exposure to my own satisfaction, for in all the cases of atopic eczema that I have studied the patients have given evidence of marked polyvalent sensitivity, and I have never been able to carry out elimination of inhalants simultaneously with elimination of foods and with other elimination tests. It is obvious that in these cases one cannot expect to get results by eliminating any one thing or any one group of substances. Hence, while there is no absolute proof that these disorders are due to hypersensitivity, one can say that the patients show hypersensitivity to cutaneous tests, and I believe that a perfection of methods for elimination of inhalants and foods may bring more satisfactory results. More encouraging is the fact that patients with atopic eczema often respond well to change of environment, and if possible they should have such a change. This points to a sensitivity to environmental factors. Unfortunately, it is often impossible to change the environment. Some of my patients have reacted well to a combination of therapy, and in the early attacks almost all have reacted well to roentgen therapy. In some cases we have checked (not cured) the disorder by giving repeatedly a mild dose of ultraviolet ray therapy, care being taken never to approach the erythema dose. In addition, we have obtained fairly good results with the ordinary stock "catarrhal" and other vaccines and with sedatives and preparations affecting the autonomic nervous system. But all in all, as a group there are many cases of atopic eczema in which the disorder is refractory to all known methods of therapy, and these present a distressing and as yet unsolvable therapeutic problem.

DR FRED WISE, New York. I suggest two therapeutic procedures with which I have had some success. The most important procedure is application of splints on the arms and legs, these are to be used regardless of the patient's objections. I have seen cases in which the use of splints alone cleared up 75 per cent of the lesions. Another measure is administration of a preparation of belladonna, this combined with phenobarbital has, I think, a better effect than any other drug or combination of measures.

DR TOULMIN GAINES, Mobile, Ala. I suggest that during recurrences the patient be given intravenous injections of strontium bromide.

DR S S GREENBAUM, Philadelphia. I think that the members all agree that in cases of this sort there is more than one etiologic factor. The nervous element undoubtedly plays a large rôle, and whether this nervous influence is central or peripheral (autonomic nervous system) makes little difference. This element in this type of condition must be controlled in all respects if good results are to be obtained. Sedatives produce bad results in some cases, in others they are helpful. In one case I used strontium bromide intravenously four times daily for fifteen days and obtained a perfect result, which, I believe, was due to the fact that the vicious circle with the nervous instability as a link was destroyed.

DR T W MURRELL, Richmond, Va. Last fall I was a patient in a hospital, and I was rubbed with alcohol so frequently that there developed a dermatitis, which did not heal. Anything that was applied seemed to make the disorder worse, and finally I went down to Virginia Beach. It was in the winter, and I could not go into the surf, but I took salt water baths in the hotel, and that gave me complete relief. Any one can get some sea salt and use it in ordinary water, making a solution of about the strength of sea water. I have been impressed by the relief obtained. This is not a cure for allergic eczema, but it helps greatly in relieving the itching.

CHRONIC TULAREMIA (?) WITH AXILLARY ADENITIS

Mrs V W, aged 42, in 1930 had an infection of the left hand after she dressed a rabbit. Shortly afterward there appeared enlargement of the glands in the axilla and neck, and recently the glands in the right axilla became enlarged. The glands in the left axilla have been draining since 1931. A cutaneous test gave a questionable positive reaction for tularemia, but there were no agglutinins nor opsonins for *Bacterium tularensis*. Culture of material from a gland showed only staphylococci. For the past two years the patient has received staphylococcus vaccine therapy from Dr Foshay. Recently she has received considerable roentgen radiation over the axillary glands. For the past fifteen years she has had a moderate diabetes, because of which insulin medication and dietary restrictions are necessary. At times she has had pyoderma and furunculosis. She claims that she had rickets and osteomalacia in early childhood. In 1924 tetanus developed after an automobile accident.

The patient has one child who is well except for "eye disease." Otherwise, the family history is irrelevant.

The skin shows pyodermic lesions with secondary excoriations. There are no local reactions to insulin. Matted glands and sinuses are present in the axillae.

Physical examination gave essentially negative results, there was no evidence of marked vascular sclerosis.

The Wassermann reaction was negative. The patient has had hyperglycemia at times. Cutaneous tests for tularemia and a tuberculin test gave negative results. The spinal fluid was normal.

Biopsy showed acute and chronic inflammatory changes. No specific granuloma and no organisms were seen in the sections.

There has been little improvement in the condition. The patient is receiving roentgen therapy. Complete excision of the glands has been recommended.

DISCUSSION

DR MAX S WIEN, Chicago. This patient is presented with a diagnosis of chronic tularemia with a question mark, and with the statement that there were no agglutinins nor opsonins for *Bact tularensis*. If this patient had tularemia she would have a positive reaction to a test for that disease. The axillary involvement presents a clinical picture almost identical with that exhibited by a patient whom I presented before the Chicago Dermatological Society (*ARCH DERMAT & SYPH* 31 150 [Jan] 1935), who had a positive reaction to the Frei test and an associated genito-anorectal syndrome of lymphogranuloma inguinale.

I think that the possibility of the axillary lesions' being due to the virus of lymphogranuloma inguinale must be considered in this case and that a Frei test should be done.

DR NORMAN TOBIAS, St Louis. I suggest the diagnosis of sporotrichosis in this case, because of the resemblance of the disorder to that in a patient I am taking care of at present. Has the pus been examined for *Sporotrichum*?

DR W H GOECKERMAN, Los Angeles. I suggest the diagnosis of acarophobia with secondary cutaneous lesions resulting from scratching. The patient told me that she had worms which she picked out of the skin.

DR MARION B SULZBERGER, New York. I agree with Dr Goeckerman. The patient said that she found little white worms in all the lesions and that these lesions "worked" and itched until she picked the worms out. Furthermore, she has anesthesia of the larynx and a reduced corneal reflex. I think that the diagnosis of acarophobia is certain but that it does not quite account for the axillary lesions and that there may well be a second disorder. I think the facts that the examination gave negative results for *Bact tularensis* and that the serologic and cutaneous tests were negative practically excludes the possibility of tularemia.

DR JOHN ERIC DALTON, Indianapolis. I agree with Dr Wien that the possibility of lymphogranuloma inguinale should be considered and that a Frei test

should be made. This case emphasizes again the importance of watching for cutaneous manifestations associated with this venereal entity. It has been my experience and that of my co-workers in about two hundred and fifty cases of lymphogranuloma inguinale that in certain cases, aside from the glandular picture, there are outbreaks of purpura, erythema nodosum and generalized papulopustular lesions, which, in certain respects, simulated a papulonecrotic tuberculid.

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DISCUSSION

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DR MARION B SULZBERGER, New York. I should like some suggestions as to the diagnosis. I can see no reason for calling this disorder atopic eczema. There

is no familial history of allergy, and that is one of the things on which the diagnosis of atopic dermatitis is based. The cutaneous tests have been negative, and that is a second point on which the diagnosis of atopic conditions is based. Furthermore, there was no demonstration of antibodies and none of eosinophilic cells. In my opinion this patient's condition should be classed in the vague group that is called "infantile eczema", I am not able to tell whether it is the contact type or the seborrheic type, but it seems to me that the disorder is not an atopic dermatitis.

ATOPIC ECZEMA

M. C., a girl aged 18, since early childhood has had cutaneous eruptions, characterized by periods of improvement and relapses, the eruptions occurring chiefly about the face, shoulders and upper extremities. In 1931, after the patient sustained an injury to the head, this eruption seemed to become much more severe and resistant to therapy. This injury also produced a partial detachment of the retina of the left eye. There are no symptoms associated with the cutaneous eruptions except "nervousness". For the past five years the patient has complained of episodes of typical hay fever occurring in the latter part of the summer and persisting until the end of September. The cutaneous condition is aggravated during these episodes. This summer (1935) she has had only slight attacks of sneezing, she was at that time receiving a course of treatment with the Kettering hypertherm. In 1933 the patient attempted suicide because of the severity of her cutaneous condition. She has frequently been hospitalized for observation. Tonsillectomy was performed in 1933.

There is no family history of any allergic reactions in the parents. A younger brother of the patient also has eczema. In one sister a cutaneous reaction results from wearing certain necklaces. One brother has no allergic history. There is no family history of syphilis or tuberculosis.

Physical examination gave negative results save for the detachment of the retina on the left.

The patient has been seen in all phases of the disorder, ranging from a generalized vesicular relapse with secondary impetiginization to a dry clear skin.

Studies of the blood gave negative results except for a persistent eosinophilia, the percentage of eosinophils ranging from 8 to 14 per cent. Urinalysis and roentgen examination of the skull gave negative results. In scratch tests with concentrated antigens positive reactions were obtained to the following foods and pollens: banana, rice, orange, cantaloup, tomato, celery, peach, grape, corn, orris, ragweed (strongly positive). Tests with the other common and uncommon food and pollen antigens were negative. Tests with the antigens which produced positive reactions were repeated after one year, and the reactions were all persistently positive. Patch tests with simple pollen and pollen oil of ragweed gave negative reactions. Patch tests with nickel and various cosmetic preparations likewise gave negative reactions.

No biopsy was made.

After a period of observation of about three years the following conclusions seemed justified: 1. Improvement of the cutaneous condition resulted simply from hospitalization, irrespective of local and systemic therapy. 2. Irritability in family life was considered an important factor in producing relapses. 3. Elimination diets plus application of coal tar ointment appeared to be the best practical temporary substitute for hospitalization. 4. Treatments with the hypertherm reduced the severity of hay fever this year, but they had no effect on the atopic eczema.

DISCUSSION

DR R. G. SENOUR, Cincinnati: This is the type of disorder regarding which I, as a younger member of the dermatologic group, should like to obtain more information. Often these cases are passed over without discussion as to therapeutics.

DR MARION B. SULZBERGER, New York: In this case I am inclined to agree with the diagnosis of atopic dermatitis. The question of therapy is difficult. As a

is discontinued almost invariably breaks down, the process again becoming active. This reactivation can be explained by the fact that in this scarring Donovan bodies have been found. I believe that the best combination of methods in cases of this disease consists in using antimony therapy until scarring takes place and then removing the scar with electrocoagulation and treating the whole area intensively with roentgen radiation.

LYMPHOGRANULOMA INGUINALE LATE STAGE OF SYPHILIS

W. C., a Negro aged 29, states that about eight months ago there developed a "sore on his penis," which kept ulcerating and eroding away until at present the penis is almost all gone. He was treated at a clinic and was using some "stuff" himself. He was operated on at the workhouse. He states that he had gonorrhea once but has had no chancre and no hair cut.

There is no history of tuberculosis or cancer in his family.

There is a scar over the left labia pudendi. Examination of the mouth shows caries and pyorrhea. In the right groin there are two scars, each about 1 by 2 cm. There is bilateral inguinal adenopathy. The penis is missing. There are ulceration and erosion of the base, which is about 0.5 cm long, it is covered with green, foul-smelling exudate mixed with red granulating tissue.

In January 1929 and in August 1935 the Wassermann reaction was 4 plus. On Oct. 23, 1935, the blood count showed 5,550,000 erythrocytes and 6,500 leukocytes.

No biopsies were made.

The patient has received ten injections of neoarsphenamine, a total of 5 Gm.

DISCUSSION

DR. SAMUEL GOLDBLATT, Cincinnati: This patient was treated with electrocoagulation, and healing resulted in six weeks. At present little can be seen of the previous lesions.

HEMANGIOLYMPHANGIOMA WITH ELEPHANTIASIS

N. C., a girl aged 20 months, is presented from the orthopedic service of the Cincinnati General Hospital. The deformity has been present since birth. The child was born normally at term, she started to walk at 13 months and to talk at 18 months. There has been no sickness. There is no familial history of any similar conditions. Three other children are living and well. The mother had edema of the left leg at the time of the birth of the patient. Examination gave negative results except for changes in the cutaneous and subcutaneous tissues.

The skin is bluish, there are doughy swellings on the right side of the body, extending from the trunk through the right labium majus pudendi and the entire right lower extremity. The right foot and leg are considerably larger than the left. Nervi are present over both thenar eminences.

The Kahn test was negative. Roentgenograms of the right leg and foot and the lower portion of the spine and the pelvis showed no changes in the bones.

Several plastic operations on the right foot have been performed by Dr. Freiberg.

Biopsies showed areas of hemangioma with some increase in fibrous tissue, some areas showed angioma resembling lymphangioma.

DISCUSSION

DR. M. J. REUTER, Milwaukee: I thought of the possibility of an arteriovenous fistula.

DR. LEON GOLDMAN, Cincinnati: My co-workers and I have examined the child carefully, but we can find no evidence of an arteriovenous fistula. The

DR LESTER HOLLANDER, Pittsburgh I heard Dr Sulzberger mention the use of ultraviolet radiation in cases of this disorder. Many of the patients exhibit involvement of the neck and arms and apparently have a photosensitivity, and I think that in view of that possibility it might be well to avoid the use of ultraviolet therapy.

DR EARL EATON, Buffalo Recently I had two patients with involvement around the face and neck, and small doses of ultraviolet radiation seemed to make the disorder worse. Three or four drops of solution of potassium arsenite three times a day appears to be helpful in some cases.

DR LOUIS A. BRUNSTING, Rochester, Minn. My co-workers and I have recently observed six patients with this kind of neurodermatitis of atopic type in whom the tragic complication of ocular cataract has developed. One patient is aged 35, the other five are of adolescent age. In three there appeared to be a decided parallel relationship between the flare-ups of the cutaneous disorder and progressive loss of vision. The cataract, which is at first subcapsular, may proceed gradually to involve the entire substance of the lens, in two of the aforementioned patients there has been almost total loss of vision. If the usual exacerbations of the neurodermatitis are subdued or brought under control by careful management or possibly by change of environment, there may be no further progression of the cataract. Cataracts of this type can be detected in the incipient stage by careful ophthalmologic examination with the aid of the slit lamp, and it seems desirable to make such studies more generally in cases of neurodermatitis.

DR WILLIAM H. GOECKERMAN, Los Angeles So much has been heard about allergy in the last ten to fifteen years that whenever one sees such a disorder one wonders whether it is due to sensitization to protein. In one case in which the patient had been treated carefully but no result had been obtained I advised the patient to see a good internist. The patient was hospitalized, and the internist made careful studies of the blood and reported that he thought the patient's blood showed that he was not getting enough proteins, in spite of the fact that he seemed to be eating a well balanced diet. He was given a diet with an extremely high protein content. Within a few days his symptoms had practically disappeared. He remained in the hospital for a few weeks, the disorder cleared up completely and did not recur. Seemingly the entire result is due to the high protein diet. Whether this affects the nervous system or not I do not know.

MYCOSIS FUNGOIDES

N. P., a man aged 62, says that his cutaneous condition has been present for four years and that it has become worse during the last two years.

The patient's father died at 77 of pneumonia, his mother died at 68 of cerebral hemorrhage. Two brothers are living and well.

Erythematous, eczematoid and nodular infiltration is present over the entire body. An involvement representing an early stage of tumor is especially noticeable on the neck.

Physical examination showed generalized vascular sclerosis, chiefly arteriolar with hypertension, without congestive failure.

Serologic tests and urinalysis gave negative results. The results of the differential count were as follows: leukocytes, 11,200, polymorphonuclears, 68 per cent, lymphocytes, 18 per cent, eosinophils, 13 per cent, mononuclears, 1 per cent.

Biopsy showed extensive infiltration in the upper portion of the corium, this consisted of lymphocytes, eosinophils and so-called lymphoblasts. There also appeared to be considerable increase in the connective tissue.

The patient has received roentgen therapy and four intramuscular injections of chaulmoogra oil.

DISCUSSION

DR ELMORE B. TAUBER, Cincinnati This patient exhibits a rather classic picture. He had a premycotic stage of the disorder, but at present he has macules

DR ARTHUR R. WOODBURN, Grand Rapids, Mich. I think one must consider in this case a combination of lesions which was recognized long before lymphogranuloma inguinale, it consists of perirectal abscesses and fistulas with secondary sinus tracts similar to these seen in this case over the buttocks and vulva. I wish to suggest this possibility.

DR SAMUEL GOLDBLATT, Cincinnati. I saw this patient for the first time six years ago, when she had a maculopapular eruption suggestive of syphilis. The Wassermann reaction was negative on several occasions at that time, and it has remained so ever since. At that time there was only a small involvement of the labia pudendi, that is to say, a slight swelling for which no cause could be found. The patient was not seen for the next five years, and when she was seen again, almost a year ago, the tremendous increase in size of the labia majora pudendi had developed. The Wassermann reaction is still negative. While the patient has undoubtedly had many opportunities for contracting syphilis as well as lymphogranuloma inguinale, I cannot believe that lymphogranuloma inguinale is present in this case in the face of the many negative Frei tests. It is certainly extremely rare to find anergy both for syphilis and lymphogranuloma inguinale in the same patient extending over a period of years. Clinically, the patient had syphilis six years ago, and clinically she has lymphogranuloma inguinale now. However, the laboratory tests were negative six years ago and have remained negative.

aspirated pus taken on the seventeenth day after the onset of acute symptoms and gave a strongly positive cutaneous reaction in four proved cases of the disease and a negative reaction in controls. Dark-field examination, smears and cultures of aspirated pus showed no pathogenic organisms. Cultures of tissue in Tyrode's medium were positive for the cultivation of a virus (Dr Joseph Tamura). Heated cultured antigen gave a positive cutaneous reaction in seven proved cases.

Cutaneous tests with Frei antigen were made on members of the immediate family. The mother and a male roomer had strongly positive reactions, the father and the aunt had negative reactions.

Vaccine therapy with cultured antigen was started on the twenty-sixth day after the onset. The temperature, which had ranged between 101 and 102 F since admission, had returned to normal. The glands at that time gave every indication of breaking down and again required aspiration two days after the administration of vaccine was started.

The vaccine was given subcutaneously on alternate days, a total of 10.25 cc. being administered in a course of twenty-two inoculations. The initial amount was 0.2 cc., this was increased or decreased by 0.05 cc., depending on the previous local reaction. The maximum dose was 0.65 cc. No objectionable reactions were noted. Thirteen days later the child's condition had improved so much that she was discharged. The glands at this time showed only a small area of induration. The patient did not come to the clinic, and several months later both glands again broke down and drained. No rectal stricture has developed.

DISCUSSION

DR SAMUEL GOLDBLATT, Cincinnati. This patient, I believe, is one of the youngest in whom the occurrence of lymphogranuloma inguinale has been reported. This disorder is peculiar in that it produces bilateral involvement of the inguinal lymph nodes in a female. This is an exceptional occurrence. The patient was treated with a specific type of serum and apparently made a good recovery, but a relapse occurred, and the child was then treated by partial excision and electrocoagulation of the involved glands.

LYMPHOGRANULOMA INGUINALE LATE STAGE OF LATENT SYPHILIS

R. F., a Negress aged 25, was treated for lymphogranuloma inguinale with sodium antimony biscatechol-di-sulfonate at the Cincinnati General Hospital five months ago. She again has a swollen labium, and there is no history of exposure. The condition started as a split in the labium, but this has now healed. The menses are regular. The patient had lymphogranuloma inguinale five years ago, this cleared up while she was at the workhouse. She has had three miscarriages. There is no history of gonorrhea.

The right labium minus pudendi is the seat of a granulomatous eruption extending about 5 cm. into the vagina and 3 cm. in length. On the surface apposing this labium minus on the right, the ulceration extends into the fold and up on the labium majus for an area of about 5 cm. The patient has lost 7½ pounds (3.4 Kg.) in the last few weeks, has felt weak and nervous and has complained of slight stinging on urination.

DISCUSSION

DR SAMUEL GOLDBLATT, Cincinnati. The patient is presented because of therapeutic results. She was treated by deep coagulation of the entire lesion, and there has been no recurrence during a fairly long period. For several years she had been treated with antimony and potassium tartrate and with sodium antimony biscatechol-di-sulfonate, but there were constant recurrences. Electrocoagulation has been used by my colleagues and me for several years, and we have not seen a recurrence after its use.

DR JOHN E. RAUSCHKOLB, Cleveland. Antimony therapy causes lymphogranuloma inguinale to heal with a thick keloidal scar, which when this therapy

Directory of Dermatologic Societies *

INTERNATIONAL

NINTH INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY
American Secretary Dr Howard Fox, 140 E 54th St, New York

FOREIGN

BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY
(CANADIAN BRANCH)

H A Dixon, President, Medical Arts Bldg, Toronto, Ont
Norman Wrong, Secretary-Treasurer, Medical Arts Bldg, Toronto, Ont

ROYAL SOCIETY OF MEDICINE, SECTION OF DERMATOLOGY

H W Barber, President, 7, Devonshire Pl, London, W 1
Louis Forman, Secretary, 7, Devonshire Pl, London, W 1

NATIONAL DERMATOLOGIC SOCIETIES

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION
ON DERMATOLOGY AND SYPHILOLOGY

Paul A O'Leary, Chairman, 102 Second Ave, S W, Rochester, Minn
J Bedford Shelmire, Secretary, 1719 Pacific Ave, Dallas, Texas
Place Atlantic City, N J

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

Howard Fox, President, 140 E 54th St, New York
C Guy Lane, Secretary, 416 Marlborough St, Boston

AMERICAN DERMATOLOGICAL ASSOCIATION

C Guy Lane, President, 416 Marlborough St, Boston
F D Weidman, Secretary, University of Pennsylvania, Philadelphia
Place New Ocean House, Swampscott, Mass Time June 4-6, 1936

SECTIONAL DERMATOLOGIC SOCIETIES

CENTRAL STATES DERMATOLOGICAL ASSOCIATION

Samuel Goldblatt, President, 3208 Colerain Ave, Cincinnati
Raymond G Senour, Secretary-Treasurer, 19 W 7th St, Cincinnati
Place Cleveland Time Dec 5, 1936

MISSISSIPPI VALLEY DERMATOLOGICAL SOCIETY

Samuel Goldblatt, President, 3208 Colerain Ave, Cincinnati
Raymond G Senour, Secretary-Treasurer, 19 W 7th St, Cincinnati

NORTHERN NEW JERSEY DERMATOLOGICAL SOCIETY

Henry J F Wallhauser, President, Medical Tower, Newark
Louis J B LeBel, Secretary, 165 Grant Ave, Nutley
Place Academy of Medicine of Northern New Jersey, Newark Time Third
Tuesday of January, March, May, September and November

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date

microscopic sections are interesting in that they show, in addition to areas of typical hemangioma, some areas of lymphangioma

A CASE FOR DIAGNOSIS

L V, a woman aged 50, has had swelling of the genitalia for a few months. Examination revealed scars of an old small papulo-ulcerative eruption which was diagnosed in 1929 as syphilid, although the Wassermann reaction at that time was negative. The elephantiasis was noted at that time but was not as great as at present and did not contain any sinuses. Examination on July 6, 1935, revealed elephantiasis of the labia majora pudendi extending over the right buttock. The lesion over the buttock was perforated by many sinuses which contained purulent discharge.

General examination gave negative results except for irregular, slightly unequal pupils.

The Frei test gave negative reactions on two occasions, with four antigens. Tests with human and bovine tuberculin were negative on two occasions. The Wassermann reaction was consistently negative.

The patient does not know exactly how long the condition existed before 1929, when it was first observed by me. No attempt at therapy has been made.

DISCUSSION

DR G S WILLIAMSON, Ottawa, Canada. I suggest the diagnosis of lymphogranuloma inguinale with negative anergy. This is the type of condition which one might expect to be associated with negative reactions, just as in cases of extensive tuberculosis there are negative reactions to tuberculin. This is probably due to the fact that the power to form immunologic bodies has been lost.

DR MAX S WIEN, Chicago. This case is a clinical example of the type of elephantiasis of the vulva seen in cases of lymphogranuloma inguinale, and there is, in addition, a dissecting cellulitis of the buttocks with purulent sinuses that resembles the picture in a case reported by Perlstein and me (*Lymphogranuloma Inguinale*, *M Rec* 139 288 [March 21] 1934). In our case, Frei tests made in the usual manner were also negative. A positive Frei reaction, however, was obtained by cross-testing as suggested by Wise and Sulzberger (*J A M A* 99 1407 [Oct 22] 1932).

The presenter informs me that cross-testing has not been done. I believe that if this procedure is properly carried out in this case it will probably result in a positive reaction to the Frei test.

DR MARION B SULZBERGER, New York. There are undoubtedly certain cases which have been described in the literature by Wien and others, and in Europe as well, in which the condition was proved to be lymphogranuloma inguinale and in which there was a negative Frei reaction. I have observed two such cases. Whether or not one can describe these conditions on the basis of positive or negative anergy must be determined by finding out whether or not the patients have elaborated antibodies which will neutralize the Frei antigen. One must see whether the serum of such patients will neutralize the antigen, as was done in cases of sarcoid tuberculosis with tuberculin. This must be done in this case before one can speak of positive anergy.

DR LOUIS A BRUNSTING, Rochester, Minn. Examination of the right buttock reveals a large plaque of brawny induration with multiple sinuses which probably represents an extension of the process from the original site on the vulva. I should consider this to be pyoderma in a person with low resistance to the banal staphylococcus and with secondary lymphedema. Sometimes syphilis is a part of the picture, but antisiphilic treatment alone will not bring about a cure. I suggest radical excision by cautery well beyond the most advanced border, followed after a suitable interval by plastic repair and grafts.

LOCAL DERMATOLOGIC SOCIETIES

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

Dudley C Smith, President, University of Virginia Hospital, Charlottesville, Va
Francis A Ellis, Secretary, 104 W Madison St, Baltimore

BRONX DERMATOLOGICAL SOCIETY

Paul Gross, Chairman, 35 E 84th St, New York
Henry Silver, Secretary, 290 West End Ave, New York

BROOKLYN DERMATOLOGICAL SOCIETY

Samuel Hecht, President, 679 Greene Ave, Brooklyn
Mortimer J Cantor, Secretary, 907 St Marks Ave, Brooklyn
Time Third Monday of each month except June, July, August and September

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

Earl L Eaton, President, 40 North St, Buffalo
Richard L Saunders, Secretary, 333 Linwood Ave, Buffalo

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY

George M Fisher, President, 264 Genesee St, Utica
Rudolph Ruedemann Jr, Secretary-Treasurer, 214 State St, Albany

CHICAGO DERMATOLOGICAL SOCIETY

Max S Wien, President, 104 S Michigan Ave, Chicago
Reuben Nomland, Secretary, 25 E Washington St, Chicago

CINCINNATI DERMATOLOGICAL SOCIETY

Raymond G Senour, President, Carew Tower, Cincinnati
Leon Goldman, Secretary-Treasurer, Doctors Bldg, Cincinnati

CLEVELAND DERMATOLOGICAL SOCIETY

H G Miskjian, President, 856 Rose Bldg, Cleveland
E W Netherton, Secretary, 2020 E 93d St, Cleveland

DETROIT DERMATOLOGICAL SOCIETY

W G Wander, President, 509 Kresge Bldg, Detroit
G Warren Hyde, Secretary-Treasurer, 2501 W Grand Blvd, Detroit

LOS ANGELES DERMATOLOGICAL SOCIETY

N P Anderson, Chairman, 2007 Wilshire Blvd, Los Angeles
Thomas W Nisbet, Secretary, 65 N Madison Ave, Pasadena, Calif
Time Second Tuesday of each month, October to May, inclusive

MANHATTAN DERMATOLOGIC SOCIETY

Paul E Bechet, Chairman, 55 Park Ave, New York
Mihran B Parounagian, Secretary, 126 E 39th St, New York

MONTREAL DERMATOLOGICAL SOCIETY

B Usher, President, 1538 Sherbrooke St, W, Montreal, Canada
Paul Poirier, Secretary, 456 Sherbrook St, E, Montreal, Canada

NEW ENGLAND DERMATOLOGICAL SOCIETY

William P Boardman, President, 388 Marlborough St, Boston
J Harper Blaisdell, Secretary, 45 Bay State Road, Boston

Book Reviews

Nouvelle pratique dermatologique Volume I Edited by Darier, Sabouraud, Gougerot, Milian, Pautrier, Ravaut, Sezary and Clement Simon Price, 300 francs Pp 720, with 207 illustrations and 13 colored plates Paris Masson & Cie, 1936

"Pratique Dermatologique," prepared under the editorship of Besnier, Brocq and Jacquet, has been, since its publication in 1900, a monumental and standard reference work of dermatology. It is now out of date and "Nouvelle pratique dermatologique" is designed to replace it. The new system consists of eight volumes containing a total of 7,350 pages, with 2,425 illustrations and 2,156 plates in color, and has been prepared under the direction of the eight dermatologists named, with the assistance of seventy-nine other representative members of the French school of dermatology.

The first volume, which treats of general dermatologic pathology, consists of ten sections. This volume was prepared under the direction of Darier by three of his former pupils and assistants, Civatte, Flandin and Tzanck, each of whom is more or less individually responsible for certain sections of the text.

The first section considers the difficulties of classification of dermatoses and contains an interesting review of all the important classifications from that of Willan in 1798 to that of Jadassohn.

The section on the anatomy of the skin comprises 92 pages, and its completeness is notable, while numerous illustrations and 6 excellent color plates add greatly to its value.

The physiology of the skin is fully considered in a section of 90 pages. The importance of its biochemical activity has received due recognition, and there are articles of varying length dealing, among other subjects, with the role of cevitic acid, glutathione, cholesterol and the ferments of the skin, all of which furnish an excellent resume of the latest knowledge of the activity of such agents.

An extensive section dealing with the general features of cutaneous histopathology, which also contains a wealth of excellent illustrations and a number of striking plates in color, constitutes a complete reference book on this subject.

The next two sections deal with etiology and pathogenesis, a particularly interesting portion being the division presenting an analytic study of the pathogenic mechanisms underlying diseases of the skin. Tables such as one showing the differential characteristics of the reaction due to intoxication and that due to intolerance and another giving a synoptic classification of diseases of the skin may be cited as illustrative of the valuable tables and charts found in the several succeeding sections.

The last section is a brief but adequate consideration of the general therapeutic principles of dermatology.

The format of the book deserves comment. The printing, illustrations and binding are extraordinarily fine and beautiful. Altogether, the volumes in this system are the handsomest the reviewer has seen in a medical book, and he has rarely seen handsomer volumes in any other type of books. The work is evidently intended to be a worthy successor to the earlier volumes, and it fully reaches that standard.

Books Received

DI SENSIBELE CHRONAXIE Lambertus Jan Hut Groningen M de Waal, 1936

Archives of Dermatology and Syphilology

VOLUME 34

OCTOBER 1936

NUMBER 4

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THE AMERICAN DERMATOLOGICAL ASSOCIATION

OBLIGATIONS AND OBJECTIVES

C GUY LANE, M D

BOSTON

I extend to every one of the members a cordial welcome to this, the fifth, meeting of this association held in Boston. My appreciation of the honor of presiding over the deliberations of this assembly, with its notable heritage and achievements, I cannot express adequately. The founding of the American Dermatological Association in Philadelphia, sixty years ago, was really the beginning of a fully recognized and independent position of American dermatology, for at that time there were in the field of dermatology no American books, no American research work and no monographs by American authors. The meeting this year coincides with the centennial of the teaching of dermatology in this country, for in 1836 lectures in dermatology were given by Dr H D Bulkley of New York at the Broome Street Infirmary.

At the first annual meeting, in Niagara Falls, N Y, Dr James C White, the first president, greeted the members with these words:

We assemble now for the first time, prepared to present to each other our views in relation to the general interests of dermatology, to report and discuss the results of our special studies, and to form that more intimate acquaintanceship among ourselves, dermatologists of a wide country, which is so essential to mutual support and understanding.

Dr White also stated that the Association would be a meeting ground for discussion, that it would furnish opportunity for the study of cutaneous diseases as they occur on this continent and for the establishment of a uniform and simple system of nomenclature and that it would foster the general interest of dermatologists in all its relations to members of the profession and to the public. In the last-mentioned objective Dr White included medical education to insure proper instruction in dermatology and the establishment of fit hospital accommodations for patients with cutaneous disease. These were the objectives sixty years ago. Can one do better at the present time?

President's Address, read at the Fifty-Ninth Annual Meeting of the American Dermatological Association, Inc., Swampscott, Mass., June 5, 1936.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON DERMATOLOGY
AND SYPHILOLOGY

Jack W Jones, Chairman, 384 Peachtree St, Atlanta, Ga
Winston U Rutledge, Secretary, 332 W Broadway, Louisville, Ky
Place Baltimore Time Nov 17-20, 1936

STATE DERMATOLOGIC SOCIETIES

CALIFORNIA MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, DERMATOLOGY
AND SYPHILOLOGY SECTION

Thomas J Clark, Chairman, 400, 29th St, Oakland
George V Kulchar, Secretary, 450 Sutter St, San Francisco

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY

Maurice J Strauss, Chairman, 41 Trumbull St, New Haven, Conn
Edward A Abbey, Secretary, 442 Temple St, New York

FLORIDA SOCIETY OF DERMATOLOGY AND SYPHILOLOGY

J L Kirby-Smith, Chairman, 204 Laura St, Jacksonville
W M Sams, Secretary, 310 Ingram Bldg, Miami

LOUISIANA DERMATOLOGICAL SOCIETY

M T Van Studdiford, President, 912 Pere Marquette Bldg, New Orleans
R A Oriol, Secretary-Treasurer, Maison Blanche Bldg, New Orleans

MASSACHUSETTS MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Harvey P Towle, President, 453 Marlborough St, Boston
Rudolf Jacoby, Secretary, 270 Commonwealth Ave, Boston

MEDICAL SOCIETY OF THE STATE OF NEW YORK, SECTION ON
DERMATOLOGY AND SYPHILOLOGY

Louis Tullipan, Chairman, 224 E 17th St, New York
C H Peachey, Secretary, 197 S Goodman St, Rochester

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA
SECTION ON DERMATOLOGY

Abraham Strauss, Chairman, Medical Arts Bldg, Philadelphia
L G Bembauer, Secretary, 5026 Jenkins Arcade Bldg, Pittsburgh

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY
AND SYPHILOLOGY

A E Schiller, Chairman, 10 Peterboro St, Detroit
G Warren Hyde, Secretary, 2501 W Grand Blvd, Detroit

MINNESOTA DERMATOLOGICAL SOCIETY

L H Winer, President, 78 S Ninth St, Minneapolis
F W Lynch, Secretary, Lowry Medical Arts Bldg, St Paul
Time First Wednesday in October, December, February and April

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

Charles P Bondurant, President, 412 Medical Arts Bldg, Oklahoma City
Darrell G Duncan, Secretary, 914 Medical Arts Bldg, Oklahoma City

TEXAS DERMATOLOGICAL SOCIETY

J C Michael, President, 1215 Walker Ave, Houston
Everett R Seale, Secretary, 1215 Walker Ave, Houston
Place Austin

COOPERATIVE STUDIES

Secondly, the excellent work of the cooperative clinical group in syphilis indicates that it is possible to carry out similar undertakings in other subjects if proper cooperation and funds are available. The association can well stimulate and even sponsor such cooperative clinical committees in pooling their resources in the study of industrial dermatoses, cancer of the skin, tuberculosis of the skin, etc. The benefits to be derived from cooperation are incalculable. Of immediate interest is the report of a committee for the study of industrial dermatoses which was appointed at the meeting of the Section on Dermatology and Syphilology of the American Medical Association in 1935.

The Section on Dermatology and Syphilology at the meeting of the American Medical Association in Kansas City, Mo., in 1936 adopted the report of this committee, which recommended

- 1 That the committee continue the study of occupational dermatoses in cooperation with the American Dermatological Association, the Section on Industrial and Preventive Medicine and Public Health of the American Medical Association and the United States Public Health Service

- 2 That a "central clearing house" be established for the recording and dissemination of information on industrial dermatoses

- 3 That subcommittees be formed in various geographic districts to gather information and report to this central committee.

The incidence of occupational dermatoses, and the losses of time, payment of wages and compensation, etc., require that such a study be carried out in a cooperative way, and if dermatologists do not participate actively it is certain that the program for handling cases of these disorders will be dictated by political lay organizations, insurance companies, state health or labor departments or federal health authorities without regard to the point of view of dermatologists. I believe that we ought to support the work of this committee in every way possible.

SYMPOSIUM

A third means of attack on these marginal subjects is the symposium. In 1902 Dr. George T. Jackson called attention to the value of groups of papers which in the ten preceding years were presented about a special subject assigned for discussion at a meeting. The presentation of three, four or five papers on different phases of one disease or one subject and possibly a comment by an invited guest cannot fail to add something of interest to the knowledge of individual members of the audience. I realize fully the limitations of subjects suitable for discussion in a symposium, but if the subjects and speakers could be selected some time in advance with the idea that definite research work would be undertaken and the literature surveyed such presentations would offer definite progress in a given subject and stimulate further investigation.

NEW YORK ACADEMY OF MEDICINE, SECTION OF
DERMATOLOGY AND SYPHILIS

Max Scheer, Chairman, 509 Madison Ave, New York

Frank C Combes, Secretary, 80 W 40 St, New York

NEW YORK DERMATOLOGICAL SOCIETY

R H Rulison, Chairman, 114 E 62nd St, New York

Eugene F Traub, Secretary, 140 E 54th St, New York

OMAHA DERMATOLOGICAL SOCIETY

J A Borghoff, Chairman, 1319 Medical Arts Bldg, Omaha

Donald J Wilson, Secretary, 1113 Medical Arts Bldg, Omaha

PHILADELPHIA DERMATOLOGICAL SOCIETY

Vaughn C Garner, Chairman, Germantown Professional Bldg, Philadelphia

Thomas Butterworth, Secretary, 238 N 5th St, Reading, Pa

PITTSBURGH DERMATOLOGICAL SOCIETY

Emerson Gillespie, President, 120 Tuscarawas St, Canton, Ohio

Joseph J Hecht, Secretary, 506 Medical Arts Bldg, Pittsburgh

ST LOUIS DERMATOLOGICAL SOCIETY

A H Conrad, President, 3720 Washington Blvd, St Louis

Roy L Kile, Secretary-Treasurer, 3720 Washington Blvd, St Louis

Place Barnard Free Skin and Cancer Hospital Time Second Wednesday of
each month

SAN FRANCISCO DERMATOLOGICAL SOCIETY

L R Taussig, President, 384 Post St, San Francisco

John M Graves, Secretary, 909 Hyde St, San Francisco

the purpose of offering to younger men the opportunities of a scientific forum and fellowship. Sections in the various special fields were created, papers were read and discussed, and clinics were held. That organization has over 700 members, and the senior national societies in the different specialties with their prescribed limitations of membership have thrived at the same time. In the last fourteen years the study group or section on postgraduate instruction of the American Academy of Ophthalmology and Otolaryngology has been one of the outstanding activities and most popular features of that organization.

A similar national organization in dermatology with less strict limitations than this association, meeting yearly in the fall, would satisfy a definite demand and eventually serve a valuable educational purpose. Perhaps the time is not yet ripe for the establishment of such an organization, but I believe that the possibility should be seriously considered.

STATISTICS

The reports of the committee on statistics have not received the attention which they deserve. I believe that such reports should be continued and perhaps amplified. Results of treatment, data about one disease and other items could be subjected to statistical study with the members' cooperation. I am aware that many members consider a questionnaire as a nuisance, but the results would be valuable to all concerned. Statistical data furnish evidence not only of the frequency of certain diseases but of the changing incidence as time passes and perhaps of the need of a change in the attitude of physicians toward those diseases. It is to be regretted that so few members have participated in these surveys. Election to the association and acceptance of membership not only should be considered an honor but should carry with it a certain sense of responsibility in working with the association toward fulfilling its purposes. I hope that it will be possible to continue making such surveys from time to time.

CLINIC

The clinic held in conjunction with the meeting has been a valuable experience for the members. I have heard it said that the clinical meetings held by various local societies and also by the different regional groups allow sufficient opportunity for the exhibition of rare conditions in dermatology. The clinic conducted in conjunction with the meetings of the association may not be as essential as it was in the early years of the association's existence, but it ought not to be given up entirely. The clinics held at these meetings have always maintained a high standard and stimulated the adequate presentation of cases elsewhere. They have also served as valuable experience for the younger men and for the men in the smaller communities. It is possible that some other method or methods can be elaborated for the purpose of continuing the clinical features in connection with the meetings of the association.

We members of the American Dermatological Association in this day and age realize how far these objectives, as stated by Dr White, have approached fulfilment. We are all conscious of the defects which have arisen as educational and scientific progress in our special field has moved forward. We recognize the changing needs from one generation to another. This association has provided a definite continuity, a unanimity of action by bringing its members—us and our predecessors—together so that we could keep pace with the changes which have occurred and could make provisions for the future.

As individual physicians we are all busy with our private practice, our hospital work, our teaching, the various investigations we are carrying on and the many elements of our daily life. As a result we are apt to neglect our obligations to the association, to disregard the actual business matters which concern every society and to overlook—unless one of them affects us directly—the many problems of the day confronting members of the medical profession in general. We all need to review our aims and our obligations occasionally. At this meeting, therefore, may I present for consideration certain affairs of the association in order that we may continue to carry forward the purposes of the association and the objectives so well outlined by Dr White in 1877, restated by Dr Hyde in 1898 and amplified by Dr Stelwagon in 1900?

First of all, I desire to emphasize the need of maintaining close contact with progress in fields outside our own. This association has passed through the period of the recognition of dermatology and syphilology as a legitimate field for specialization. It has progressed beyond the period in which cutaneous manifestations were considered as being in a distinct compartment. It is of course impossible for one to keep abreast of medicine in general in such a way as to be able to bring to bear on a particular problem all the knowledge pertaining to that problem, but this association can furnish us with assistance in the solution of the many borderline problems.

THE CONGRESS

In the first place, I hope that in the near future the association will be able to rejoin the Congress of American Physicians and Surgeons and participate at least once in five years in meetings devoted to general medicine and specialties other than our own. It is my belief that the full value of participation in such meetings has been only partly realized in the past. To me it seems that such a meeting held at intervals provides the opportunity for joint discussions of a borderline topic with some special society which has a field adjacent to ours, and I believe that members of both associations will derive mutual benefit from such discussions.

time men devoting their study to problems of interest to us all. Such a fund would be under the control of the association and be used for dermatologic research. It could therefore not be transferred to any other purposes. The funds left to a university or hospital have a mysterious way of not being used always as intended.

GRADUATE TRAINING

Another obligation of the association is to aid in providing adequate training for young dermatologists. In 1881 Dr. James Nevins Hyde stated before the members of this association that a common error in vogue at that time was that the "study of diseases of the skin was the pursuit of a narrow specialty and that there was an ignorance of the functions and maladies of important internal organs", he also stated that "he who would especially devote himself to the investigation of disorders of the skin required the amplest preparation in a finished general medical education and experience."

The standards of yesterday grow into the standards of today. In accordance with the urge of progress, the Advisory Board of Medical Specialties and the Council on Medical Education have adopted somewhat higher requirements for a certificate in a specialty, which are to become effective in 1938. All the special boards have among their purposes the improvement of the standards of practice, and this elevation of the requirements is a logical feature of an attempt to improve those standards. This has been done with the full realization that it is not advisable to raise any standards or regulations abruptly to such an extent as to nullify the objects aimed at. In 1938 and thereafter in order to be eligible to take an examination of a specialty board a candidate after an internship of one year will be required to complete a three year period of study in clinics, hospitals and laboratories which bear the approval of the specialty board and of the Council on Medical Education and Hospitals of the American Medical Association. This period of study is to include an active experience of eighteen months in such institutions and adequate graduate training in the basic sciences pertinent to the specialty. Two years of further study or practice is required before examination. Examinations will be required in the basic sciences as well as in the laboratory and public health phases of the specialty.

No one doubts the value of a background of fundamental or basic science relating to the specialty. There may be differences of opinion on subjects to be classed as basic and the time allotted to each. It would seem necessary that some fundamental work be given in embryology, physiology, chemistry and bacteriology as related to the skin. Histopathology has already been largely developed, and mycology and serology are receiving adequate attention in many institutions. Pharma-

The papers on syphilis presented at this session and the discussion amply prove the value of the symposium in our program. Syphilis should always have a prominent place in the programs of this association. That disease is bound to be included in future public health programs, and we should remain in the forefront of the attack on this disease—its diagnosis, its prevention and its treatment. While the cutaneous manifestations of syphilis are said to be vanishing, it is hard to visualize the time when there will not be need of differentiating syphilis from other cutaneous conditions. More attention should be paid to syphilis in dermatologic clinics, and the general knowledge needed in the proper care of syphilis should be amplified in future programs for the training of dermatologists.

MEMBERSHIP

The proposal to increase the limit of membership in the association should receive serious attention. The association has always been a relatively small body and the members have known each other intimately. Of course there are differences of opinion on this point, but in general we have rejoiced in the congenial atmosphere of our meetings. The number of dermatologists in this country has increased greatly, and the limit of membership has been raised from 25 to 40, to 75, to 100 and to 125. It is, however, true that any great enlargement of our membership will tend to lessen the close acquaintance which we have cherished. I am not sure what the ultimate limit of the number of our members should be, but I am sure that the best interests of the association and its members will be served by retaining a relatively small membership. This association now numbers 112 active members, hence urgent action is not required on our membership limit at this meeting. It is possible that the carrying of all members of twenty years' standing in a separate class and the stricter requirements adopted last year concerning attendance and presentation of papers may postpone the need for action on the membership limit for several years. In recent years the desire for opportunities to meet one's neighbors and exchange information has brought about the formation of numerous local societies and dermatologic sections of state medical associations. That there is also a desire for membership in an organization which is more than a purely local society is demonstrated by the fact that several sectional groups have been organized, but there is only one national forum besides the American Dermatological Association, namely, the Section on Dermatology and Syphilology of the American Medical Association. If the interest in our specialty continues, the establishment of another national organization in the field of dermatology may be advisable.

It has been suggested that the members of this association participate in the formation of an American Academy of Dermatology and Syphilology, perhaps patterned along the lines of the American Academy of Ophthalmology and Otolaryngology. This was formed in 1910 with

made by graduates of these different hospitals and medical schools in the examinations by the board

It is probably not of primary importance whether this specialty training shall center about a clinic or a medical school. The basic science study as a rule can be carried out better in the medical school, but undoubtedly some of the larger departments of dermatology can provide the requisite basic training within the department. Clinics, of course, will furnish the greater part of the teaching as at present, but it will be necessary that the medical schools and the clinics cooperate in providing the necessary facilities

Three years ago a study of the diplomates who had passed the board examination showed that 75 per cent obtained their training by graduate work through residencies in dermatologic departments or by acting as assistants in offices of well known dermatologists. The other 25 per cent obtained their dermatologic training by clinical experience

In the three years of training as suggested not only must there be adequate clinical experience and actual supervised instruction in cutaneous diseases and syphilis, but adequate time and facilities must be available for students who are research minded and properly equipped to pursue individual problems as far as possible. In other words, provision must be made for two classes of students, (1) for those who will become teachers and research workers and make for progress in dermatology and (2) for those who desire only to become good practitioners in dermatology

A training of this kind will furnish an excellent background for the two years of practice or study which will be required before the budding specialist can present himself for examination and obtain full recognition as a specialist in dermatology and syphilology. I have no recommendation to make concerning this program, but I desire the members to be informed of the progress which is being made toward an objective in which all of us are interested

This problem of placing specialization on a rational graduate basis is one of the important problems facing us at the present time, and our active efforts toward its solution will result in better training of dermatologists, who can go further than we have in solving problems of etiology, in controlling and preventing disease and in providing more rational treatment for patients with cutaneous disease. Such a forward step will redound greatly to American dermatology

The objectives for which we as members of the American Dermatological Association are striving should ever remain on the high plane established by our predecessors, and in order to attain this ideal we must keep faith with our obligation to the society in order to create the obligations of the association to us as members

EXHIBIT

At the meeting of this association an exhibit has been an extremely minor matter, while the exhibit held at the meeting of the American Medical Association has always been well attended and has called forth many expressions of commendation. The custom of having at least an exhibit from the reader of each paper should be developed. Such a display of data should not detract from a paper but should round out to a considerable degree the paper in question by providing a more complete exposition of a subject than can be given in the allotted fifteen or twenty minutes of actual presentation. The discussion of a paper is often continued during the displaying of an exhibit with benefit to all concerned. I realize fully that greater effort is required, on the part both of the exhibitor and of the local committee, in the presentation of the exhibits, but the educational value of a well planned and well executed exhibit cannot be denied.

FINANCES

The report of the treasurer shows that the financial structure of the association is sound. The accumulative feature of small amounts of money is well shown by the present resources. A transfer to the permanent fund of money not immediately necessary has been recommended by the board of directors and is advisable. Furthermore, any action on dues should be based on the accumulation of a small yearly surplus to be added to the permanent fund so that the amount of income at the disposal of the research aid committee would be gradually increased. It may be argued that the dues should be used simply for the ordinary expenses of the association, but the members could well take pride in the advances resulting from the collective aid furnished by means of a research aid fund. The purpose of the association, as stated in the by-laws, is the promotion of the study of dermatology and syphilology in all their relations. The work and influence of this organization can be greatly extended if the association has at its disposal a fund for the purpose of bestowing awards for work well done or encouraging scientific dermatologic contributions by means of grants for such work.

It is time that a real attempt be made to create an adequate research aid fund from within or from without the association or from both. I believe that the research aid committee should be granted the power to raise funds to initiate a program of research work, these funds may not be adequate at first, but they would constitute at least a beginning of the participation of the association as such in active research work. A fund of \$50,000 would make it possible for the association to sponsor a fellowship for a full time man or for two or more part

These experiments were much discussed and have been the cause of violent disagreement. They have been repeated by many investigators—Mibelli, Samuel, Behrend, Bechterew, Moskalenko and Gregoriantz, Koster, Fay and Wright—some of whom denied the appearance of cutaneous lesions, while others obtained them but gave various explanations for the phenomenon.

The problem was at this stage when I returned to the aforementioned experiments and succeeded in proving that the cutaneous lesions obtained are exclusively due to trauma by scratching, which is provoked by the pruritus and hyperesthesia caused by the partial denervation of the cervicofacial region in the animal.

One hundred and eighteen experiments were made on the second cervical nerve, establishing the fact that section of the sensory tracts of that nerve in the cat produces hyperesthesia or initial pruritus and afterward the appearance of alopecia or of ulceration in the second dermatome, in the region of the skin innervated by the cut root, especially in the areas overlapping the innervation by neighboring nerves (third cervical and trigeminal). The occurrence of lesions is exceptional if ether is used as an anesthetic (4.83 per cent) but more frequent if a dextrose derivative of chloral is used (35.29 per cent). In another series of thirty-six animals, unilateral section of the first three cervical nerves was performed, and under these conditions the degree of pruritus and the frequency of alopecia and ulceration in the second dermatome or root territory of the skin increased (50 per cent).

In order to demonstrate the traumatic origin of the lesions I repeated this experiment in fourteen animals, the heads of which were protected permanently by leather caps. None of them acquired the slightest cutaneous lesion, but the caps showed evident marks of scratching. For further confirmation, when the cap was removed from one of the animals thirty-seven days after the operation, I was able to observe immediate violent scratching, which led to the rapid appearance of alopecia and ulceration.

The pruritus and hyperesthesia are of peripheral origin and appear only in the areas of common innervation between the sectioned nerves and the neighboring untouched nerves, the latter carrying the abnormal sensations to the nerve centers. This can be proved by cutting all three cervical nerves and the trigeminal nerve (which participates in the innervation of the area under observation) of the same side, which prevents the development of the pruritus and the traumatic lesions.³

3 By cutting the trigeminal nerve (with or without the cervical nerves), in addition to the classic lesions described, ulcerated pruriginous traumatic lesions, similar to those under discussion, may be produced in a different area (the preauricular, which is also innervated by the cutaneous branch of the vagus nerve).

cology, immunology, hematology, endocrinology and the physics of radiology and physical therapy certainly deserve adequate emphasis in the preparation of any person intending to specialize in dermatology

For such a minimum basic course in science the schedule, as it has been tentatively planned by the American Board of Dermatology and Syphilology, there is allotted about two hundred and fifty hours. An eight month college year provides about twelve hundred hours, hence the suggested schedule for basic work in science would occupy less than 25 per cent of a college year. This schedule could be completed in perhaps three months of the first year, or it could be extended over the whole year, coincidently with the clinical experience. Another matter under discussion is the allotting of six months in a two year residency for basic work, with the expectation that the resident will major in one of the basic sciences during this period. It is of course open to question whether it is desirable to allot a certain number of hours for each subject or whether it is best to define carefully the field to be covered in each subject, indicating its limits and allowing the details for covering the field adequately to be worked out by the individual institution and the head of the department.

The adequate fulfilment of these requirements is an objective of major interest to every member of this association. Not only does the American Dermatological Association act as sponsor for the board, but among its 123 members are the heads of dermatologic departments and dermatologic teaching staffs of all the large institutions. Eighty per cent of the members hold professorial rank, and there are only a few members who do not hold, or have not held, teaching positions. We are all, therefore, vitally interested in a program which is to become effective in 1938, or, if the opportunities are not available at that time, in 1940.

It may be that two years is sufficient, but all will agree that three full years of continuous training will provide a more comprehensive foundation. It is probable that three years, portions of which are spent at different times and at different institutions, will be accepted, provided that the equivalent of three full years of training is maintained.

Concerning the approval of clinics or institutions, it is probable that the board will have a higher standard so far as this specialty is concerned than that determined by the Council on Medical Education and Hospitals of the American Medical Association, at least at the present time. Provision for the inspection of various institutions in order to estimate their capacity for adequate training will undoubtedly be necessary and is certainly advisable, but no machinery for this function is as yet available. As the years pass an adequate guide to the value of training received in the various institutions will accumulate in the records

PRURITUS AND HYPERESTHESIA CAUSED BY PARTIAL SENSORY DENERVATION

EXPERIMENTAL ALOPECIA—A CONTRIBUTION TO THE STUDY OF ALOPECIA AREATA

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In 1933 Beeson and Pickett¹ published a contribution to the experimental study of alopecia areata

In spite of having read my publications² in which I conclusively demonstrated the physiopathologic mechanism of the cutaneous lesion obtained experimentally, the authors confined themselves to repeating on twenty-one cats Max Joseph's operation, the extirpation of the second rachidian ganglion with its corresponding roots. Their conclusions were as vague as those of Joseph, who stated in 1886 that the lesions of alopecia obtained by this operation are similar to those of alopecia areata in human patients, which gives the false impression that the nerve section causes the appearance of the disease in the animal. Besides this, they did not study the physiopathologic process leading to the experimental production of the lesions.

Without meaning to be controversial, I think it useful to publish this paper, because I feel that Beeson and Pickett, in spite of the industry which their work implies, have taken a step back in the elucidation of the mystery which shrouds the pathogenesis of alopecia areata.

Among the theories put forward to explain the origin of the disease, without doubt the most promising was that which presupposed the possibility of reproducing it in animals by section or extirpation of certain nerve roots. Max Joseph was the first to practice the ablation of the second cervical rachidian ganglion and its corresponding roots, obtaining patches of alopecia, which he said resembled pelade in human patients and which were interpreted as trophic lesions caused by section of a nerve with a specific trophic function.

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(Prof. B. A. Houssay)

1 Beeson, B. B., and Pickett, W. J. Experimental Alopecia. A Contribution to the Study of Alopecia Areata, *Arch. Dermat. & Syph.* 28: 53 (July) 1933.

2 Aubrun, E. A. (a) Pelada experimental de Max Joseph (prurito e hiperestesia por sección nerviosa), Buenos Aires, Imprenta López, 1931, vol. 1, p. 666, (b) Pelada experimental de Max Joseph (Prurito e hiperestesia por sección nerviosa), *Rev. argent. de dermatosifil.* 15: 73, 1931.

In later experiments ⁴ I also showed that extirpation of the cervical sympathetic ganglions does not produce pruritus, cutaneous lesions or lesions in the hair and that sympathectomy previous to the extirpation of the cervical roots does not modify the hyperesthesia and pruritus caused by the operation itself. The sensory alteration does not appear to be due to vasomotor changes or to the increase of permeability of the capillaries.

To summarize, I have clearly shown that the cutaneous lesions, the traumatic origin of which is undeniable, obtained in cats by section of certain nerves do not reproduce experimentally the lesions of alopecia areata, the etiology and pathogenesis of which are still unknown to me.

The practical result of my investigations was the demonstration of the existence of a new type of sensory alteration—the hyperesthesia and pruritus of peripheral origin associated with partial sensory denervation in some cutaneous areas. It remained to give an explanation for the occurrence of the pruritus, that is, to investigate the factor which produces the abnormal sensation in the areas with a common innervation by the sectioned and untouched nerves, the latter forming the efferent path to the nerve center, with the resultant reflex scratching.

In connection with this I wrote in my thesis ⁵ "The immediate appearance and periodic intensification which we have observed on several occasions lead us to suspect the existence of some local change which at the present moment we are unable to determine (metabolites)."

Thus I was inclined from the first to suspect that section of the nerve caused some substance to be liberated in the area supplied by that nerve which might cause the described phenomena. For technical reasons I have been unable to demonstrate this hypothesis, though I still consider it the only admissible explanation in the present state of knowledge.

In support of this theory I may say that the analysis of a series of works on general or special physiology during the last few years showed that the idea is gaining ground that the appearance of many physiologic and pathologic phenomena in which nerves have a leading rôle is due to the liberation of substances at a given moment. I confine myself to citing such instances as bear on my own problem.

De Waele, Vandeveldé and Braye ⁶ held that the peripheral vasodilatation observed during excitation of a posterior root is caused by antidromic propagation of the stimulus to the skin, whence, either by

4 Aubrun, E. A. Prurito e hiperestesia por sección nerviosa. Acción vascular y simpática en el prurito por desnervación sensitiva parcial, *Rev argent de dermatosifil* 16 363, 1932.

5 Aubrun, ^{2a} p 255.

6 De Waele, Vandeveldé, J., and Braye, L. L'origine et le trajet des vasodilatateurs des racines postérieures, *Bull Acad roy de méd de Belgique* 9 580, 1929.

anastomosis or by the formation of algogenic substances which spread to the surrounding areas, it ascends by the normal paths of the neighboring nerve roots to the spinal and motor centers

Foerster⁷ observed that pain occurs when the peripheral ends of certain nerves are stimulated, and he expressed the belief that it was due to the transmission of the excitation to the neighboring sensory nerves, through peripheral anastomosis. Feldberg and Schilf⁸ accounted for the pain as due to the liberation of a substance "H" (of histamine type), which on spreading through the tissues excites the sensory receptors of the neighboring undivided nerves. The latter theory finds support in the unusual duration of this type of pain.

Finally Kibjakow⁹ stated that he had found vasodilator substances, metabolites, of peripheral origin in the veins of the part corresponding to the excited posterior roots.

I hope that some special technic will be devised by which it may be proved that the sensory phenomena under consideration are due to the liberation on section of the nerves of an algogenic substance or one causing pruritus, which by its action on the untouched sensory nerve endings causes reflex scratching.

7 Foerster, O. *Die Leitungsbahnen des Schmerzgefühls und die chirurgische Behandlung der Schmerzzustände*, Berlin, Urban & Schwarzenberg, 1927, p. 20.

8 Feldberg, W., and Schilf, E. *Histamin Seine Pharmakologie und Bedeutung für die Humoralphysiologie*, Berlin, Julius Springer, 1930, p. 457.

9 Kibjakow, A. W. *Zur Frage des Vasodilatations Mechanismus bei der Reizung antidromer Nerven*, *Arch f d ges Physiol* 228 30, 1931.

CERTAIN PHASES OF SULFUR METABOLISM OF THE SKIN

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AND

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Considerable investigation has been conducted regarding the rôle that sulfhydryl compounds play in the cellular activity of normal and abnormal growth, as a factor in oxidation and reduction and as detoxifying agents. The study herein reported embraces these phases of sulfur metabolism in relation to the physiology of the skin in the normal state, in systemic pathologic states and in diseases of the skin. In previous communications¹ we reported the results of studies and reviewed data showing the important rôle that cystine plays in the formation and development of keratin-containing tissue, especially hair, wool and nails.

Sulfur in the skin exists essentially in organic combination. It is believed that a large portion is in the form of cystine and cysteine. Other known sulfhydryl compounds in the skin are glutathione and methionine.

The total sulfur content of the skin was determined rather than the amount of the individual, naturally occurring sulfhydryl compounds. Determination of the total sulfur content is more accurate and affords a composite picture of all the sulfhydryl compounds. Our purpose in this investigation was to make a general survey of the evidence indicating a disturbance of sulfur metabolism.

METHOD

The total sulfur content of the skin was determined according to the method of Frear² and is expressed as the percentage of sulfur of the dry weight of the skin. In the preparation of the specimen of skin only superficial fat was removed, preliminary to the drying operation. No attempt was made to carry out an

Read at the Ninth International Congress of Dermatology and Syphilology, Budapest, Hungary, Sept 13, 1935

From the Research Institute of Cutaneous Medicine and the Philadelphia General Hospital

1 (a) Brown, H., and Klauder, J. V. Sulphur Content of Hair and of Nails in Abnormal States, Therapeutic Value of Hydrolyzed Wool. I. Hair. *Arch Dermat & Syph* 27:584 (April) 1933. (b) Klauder, J. V., and Brown, H. Sulphur Content of Hair and of Nails in Abnormal States. II. Nails, *ibid* 31:26 (Jan) 1935.

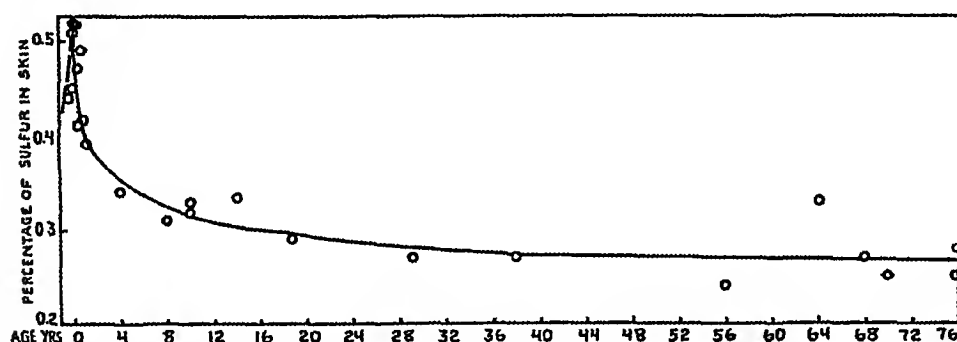
2 Frear, D. E. The Adaptation of the Benedict-Denis Method to the Determination of Sulphur in Plants, *J Biol Chem* 86:285, 1930.

exhaustive series of fat extractions designed to remove cellular lipoids. An estimation of the inorganic sulfur content was of course included in the determination of the total sulfur content. The amount of inorganic sulfur in the skin, however, is insignificant compared with the total amount of organic sulfur. The margin of error inherent in the method employed, we believe, is less than 0.1 per cent. Many of our specimens checked within 0.05 per cent. About 0.2 Gm of skin as removed from the patient was required for analysis.

The sulfur content of the skin was determined from the following sources: (1) the skin of man from infancy to old age, (2) the skin of rabbits from birth to maturity, (3) the scales and skin of patients with various skin diseases, especially psoriasis, (4) the skin obtained at autopsy from patients with systemic infections or disorders, (5) the skin of mice before and after maintenance on a diet poor in cystine, and (6) slowly and rapidly growing carcinoma in mice and malignant lesions in man.

NORMAL TOTAL SULFUR CONTENT OF THE SKIN

Specimens of normal skin from persons of various ages, from infancy to old age were obtained during life and at autopsy and examined for the total



Curve showing the percentage of the total sulfur content in the skin of man at different ages

sulfur content. Specimens from patients dying of infections, intoxications and malignant disease were not included in this group. From the results plotted in the chart it can be seen that the sulfur content of the skin decreases with age. During the first year of life the percentage of sulfur in the skin ranges from 0.40 to more than 0.50, it decreases rather abruptly the first few years of life to about 0.35, more slowly until adolescence (from 12 to 16 years), to about 0.30, and thereafter but little or not at all. The normal sulfur content of the skin of the adult appears to be from 0.25 to 0.30 per cent, the majority of the figures being between 0.26 and 0.28 per cent. We are not acquainted with any extensive reports on studies of the percentage of sulfur in normal skin from persons of different ages. Reported analyses embrace the results in one or in a few specimens of normal skin.

For the purpose of comparison, as determined in previous studies,¹ we regarded the normal percentage of sulfur in hair to range from 4.5 to 5.2, and in nails, from 3 to 3.6. In these studies we did not determine if the percentage of sulfur in hair or nails varied from infancy to old age as it does in the skin. In Payne

and Perlzweig's³ study of the cystine content of nails, no variation on the basis of age was reported. The age range of the patients, however, was from 17 to 70 years.

SULFHYDRYL AS A FACTOR IN NORMAL AND ABNORMAL GROWTH

The skins of litter mates of rabbits were analyzed for total sulfur content from birth to maturity. A series of such analyses were conducted and repeated on a second litter. It was observed that there was a nearly uniform decrease in the total sulfur content from birth to maturity. The following figures for the percentage of sulfur are representative of the results but do not represent the total number of examinations made. In animals up to 2 weeks of age the percentage was about 0.69, decreasing at the age of 3 months to about 0.54, at the age of 8 months it was about 0.46.

In a previous communication⁴ we reported the results of a study on the relation of sulfhydryl compounds to abnormal growth (mouse carcinoma). The total sulfur content of different organs of mice maintained on a normal diet and on a diet poor in cystine, the effect of such diet on the rate of growth of cancer in mice and the correlation of the rate of growth of transplanted mouse carcinoma with the sulfur content of such tumors were studied. It was concluded that there was a loss of sulfur in the muscle, liver, spleen, kidney and skin of white mice maintained on a diet poor in cystine, that transplanted tumors grew more slowly in mice maintained on such a diet than in mice on a normal diet, that the rate of growth of mouse carcinoma correlated the sulfur content and that regardless of the factors involved in retarding the rate of growth of the tumors in the animals studied, the sulfur content correlated the rate of growth.

In the study reported here we determined the total sulfur content of benign and malignant lesions involving the skin as well as of malignant tissue involving different viscera in man. The total sulfur content of malignant tissue was compared to the total sulfur content of the normal tissue from which the malignant growth arose. It was observed that benign (nonhairy) melanoma of the skin generally had a high sulfur content. The percentage of sulfur in each specimen examined was as follows: 0.20, 0.39, 0.60, 0.69, 1.05 and 0.29. Malignant melanomas of the skin contained a still greater percentage of sulfur. The percentage in each specimen examined was as follows: 0.50 (surrounding normal skin, 0.27), 1.06, 0.74 and 0.93. Two different specimens of epithelioma of the skin contained 1.2 and 0.81 per cent of sulfur, respectively. A study of the percentage of sulfur in malignant tissue from various viscera did not show uniformly a greater percentage of sulfur than that contained in the organ from which malignant growth arose. Results of the study were not as striking as those obtained in the aforementioned similar study of mouse carcinoma. In the latter study it is to be noted that the animals were exsanguinated prior to examination of different tissue, and hence such tissue was examined free from blood, whereas difficulty was experienced in completely removing blood from specimens obtained from human beings at autopsy.

3 Payne, S. A., and Perlzweig, W. A. Cystine Content of Finger Nails in Pellagra, *J. Clin. Investigation* 12: 899, 1933.

4 Brown, H., and Klauder, J. V. Total Sulphur of Tissue in Normal and Abnormal Growth (Mouse Carcinoma), *J. Lab. & Clin. Med.* 20: 1143, 1935.

The skin of ten patients dying of cancer was examined for the total sulfur content. The percentage of sulfur was below normal in four of these specimens, ranging from 0.17 to 0.23, in two it was 0.25 (low normal), and in four it was normal.

Comment—The conclusion reached in our study that the sulfur content of the skin decreases with age both in rabbits and in man is in accordance with the knowledge of the rôle that sulfhydryl plays as a growth factor. Cystine, the oxidized form of the sulfhydryl-containing amino-acid cysteine, is one of that limited group of amino-acids which is indispensable for normal growth and development. In Thompson and Voegtlin's ⁵ study of the glutathione content of the organs of the white rat it was observed that the amount of glutathione decreased with the age of the animal. Binet and Magrou ⁶ made similar observations pertaining to the glutathione content of the liver of rats, and Crosti ⁷ also found the same to be true of the glutathione content of the skin of rabbits and rats.

Our observation that the rate of growth of mouse carcinoma correlated the sulfur content and that some malignant lesions in man contain more sulfur than the organs in which they arise is likewise in accordance with the knowledge of the rôle that sulfhydryl plays as a growth factor as embraced in the hypothesis of Hammett and his co-workers ⁸. Reimann and Hammett ⁹ have reported gross acceleration of wound healing by the simple external application not only of cystine but also of thiodextrose and thiocresol. Reports of other investigators as to whether malignant tissue contains more glutathione than the surrounding normal tissue have been conflicting.

Our observation of the high total sulfur content of benign and malignant melanoma is in accordance with the observation of others that some melanins are rich in sulfur. This may have some significance in view of the well known fact that a malignant melanoma is highly malignant.

5 Thompson, J. V., and Voegtlin, C. Glutathione Content of Normal Animals, *J. Biol. Chem.* **70**:793, 1926.

6 Binet, L., and Magrou, J. Composés du soufre et croissance, *Presse méd.* **40**:853, 1932.

7 Crosti, A. Alcune osservazioni sul glutathione nella pelle e su suoi metodi di ricerca, *Gior. ital. di dermat. e sif.* **73**:1526, 1932.

8 Hammett, F. S. The Chemical Stimulus Essential for Growth by Increase in Cell Number, *Protoplasma* **7**:297, 1929. Hammett, F. S., and Reimann, S. P. Cell Proliferation Response to Sulphydryl in Mammals, *J. Exper. Med.* **50**:445, 1929.

9 Reimann, S. P., and Hammett, F. S. Cell Proliferation Response to Sulphydryl in Man, *Proc. Soc. Exper. Biol. & Med.* **27**:20, 1929.

TOTAL SULFUR CONTENT OF THE SKIN OF PATIENTS WITH SYSTEMIC INFECTIONS AND DISORDERS

Skin removed at autopsy from ten patients dying of pulmonary tuberculosis was examined. The percentage of sulfur in seven specimens was low, ranging from 0.21 to 0.24, whereas it was normal in the remaining three. The results of this study are shown in table 1.

The skin of ten patients dying of chronic or acute infection was likewise examined. Chronic infection embraced bacterial endocarditis, acute infection embraced chiefly pneumonia, acute appendicitis and acute meningitis. The percentage of sulfur was low in three specimens (0.21, 0.24 and 0.39, the last being the percentage obtained in an infant aged 1 year) and low normal (0.25 and 0.26) in two. In the remaining five specimens the percentage of sulfur was normal. The skin of twelve patients dying of diabetes mellitus, or its complication, showed a normal range of percentage of sulfur.

TABLE 1—*Low Percentage of Sulfur in the Skin of Patients Dying of Pulmonary Tuberculosis*

Case	Sex	Color	Age	Postmortem Diagnosis	Percentage of Sulfur of Dry Weight of Skin
1	M	W	56	Pulmonary tuberculosis	0.24
2	F	C	21	Miliary tuberculosis, chronic ulceration	0.28
3	F	W	26	Tuberculosis, pneumonia, diabetes	0.21
4	F	O	30	Diffuse ulcerative pulmonary tuberculosis, tuberculous ulcerations of intestines	0.23
5	F	O	20	Tuberculous bronchopneumonia	0.24
6	M	W	50	Pulmonary tuberculosis cavitation with bronchopneumonia	0.27
7	F	W	34	Fibrocaceous pulmonary tuberculosis	0.24
8	F	O	22	Pulmonary tuberculosis	0.24
9	F	C	21	Chronic ulcerative pulmonary tuberculosis, tuberculous enteritis and peritonitis	0.25
10	M	W	51	Bilateral pulmonary tuberculosis with miliary spread	0.24

In this group was included the skin of four patients with pellagra, all of whom had cutaneous manifestations, the disease in two was severe. The percentage of sulfur in three of these specimens was low and low normal, 0.22, 0.25, 0.26 and 0.29.

The percentage of sulfur in the skin of four patients with arsphenamine dermatitis and one patient with dermatitis due to the ingestion of a gold compound was definitely low, ranging from 0.20 to 0.22.

Comment—Our findings of a low and low normal sulfur content of the skin in one half of our series of patients dying of acute and chronic infections and in the majority of those dying of tuberculosis is in accordance with our knowledge that sulfur metabolism plays a defensive rôle and that cystine and glutathione are important detoxifying substances.

In studies of Robin and Bournigault¹⁰ it was observed that the total sulfur content was decreased in tissues considerably involved by tuberculosis.

10 Robin, A., and Bournigault, A. *Le soufre dans le foie cancéreux*, Bull Acad de méd, Paris 83 178, 1920.

To explain the presence of a low percentage of sulfur in the skin of patients with systemic infections, carcinoma and other chronic systemic disorders it would be desirable to correlate such findings with the results of studies of sulfur balance. Evidence has been reported of a disturbance of sulfur metabolism during fever and in cancer and tuberculosis.

Sullivan and Hess¹¹ noted a decrease in the cystine content of the nails of patients with arthritis and attributed this to the demands made on the organism for sulfur as a detoxifying agent. In Payne and Perlzweig's³ study it was observed that the cystine content of nails was decreased in patients with pellagra who presented a severe dermatitis. It is to be recalled that evidence has been submitted (Camurri,¹² Koch and Voegtlin¹³ and Smith¹⁴ that the metabolism of sulfur is abnormal in pellagra, and Sabry¹⁵ has reported favorable results in the treatment of this disease with sodium thiosulfate.

In a previous study^{1b} on the total sulfur content of nails we reported a low percentage of sulfur in the nails of patients with chronic pulmonary tuberculosis, chronic arthritis of the deforming type, pernicious anemia, inoperable carcinoma and pellagra and of patients with prolonged fever secondary to systemic infection.

Our observations of a definitely low percentage of sulfur in the skin of three patients with arsphenamine dermatitis is in line with the observations reported by Voegtlin, Dyer and Leonard¹⁶. In their studies experimental evidence was presented indicating that the action of arsenic on protoplasm is essentially due to an action on certain organic sulfur compounds containing sulfur in the mercaptan (sulfhydryl) form. This conclusion was based on the following facts: 1. Arsenic tri-oxide and its organic derivatives readily combine in vitro with hydrogen sulfide or certain sulfhydryl compounds with the formation of condensation

11 Sullivan, M. X., and Hess, W. C. Studies on the Biochemistry of the Cystine Content of Purified Proteins, *Pub Health Rep*, supp 86, 1930, p. 1

12 Camurri, V. L. *Atti d Cong pellagrol ital*, 1910, p. 67, cited by Kahn, M., and Goodrich, F. G. *Sulphur Metabolism*, Philadelphia, Lea & Febiger, 1926

13 Koch, M. L., and Voegtlin, C. Chemical Changes in the Central Nervous System as a Result of Restricted Vegetable Diet. II Chemical Changes in the Central Nervous System in Pellagra, *Bulletin 103*, United States Public Health Service, Hygienic Laboratory, 1916

14 Smith, J. H. The Influence of Solar Rays on Metabolism, *Arch Int Med* 48:907 (Nov) 1931

15 Sabry, I. Ueber die chemische Natur des Pellagratoxins und die Entdeckung der Thiosulfatbehandlung der Pellagra, *Dermat Wchnschr* 96:265, 1933

16 Voegtlin, C., Dyer, H. A., and Leonard, C. S. On the Specificity of the So-Called Arsenic Receptor in the Higher Animals, *J Pharmacol & Exper Therap* 25:297, 1925. The Mechanism of the Action of Arsenic upon Protoplasm, *Pub Health Rep* 38:1882, 1923

products 2 All protoplasm with an active metabolism contains sulfhydryl compounds, as indicated by a positive nitroprusside test 3 The toxic action of arsenoxide on trypanosomes in test tube suspensions and in the living rat can be completely inhibited by supplying an extra amount of certain sulfhydryl compounds (cysteine, thioglycollic acid, glutathione, glycylcysteine and thiosalicylic acid) 4 The toxic action of arsenoxide on rats is diminished by a previous injection of thioglycolate, as shown by the fact that these animals survived longer than the controls that received arsenic only

Voegtlin and Thompson¹⁷ have shown that the arsenic of arsenoxide is tenaciously retained by the body of the albino rat and that the drug disappears fairly rapidly from the blood, which is evidence that the arsenoxide has a great affinity for tissues As Voegtlin points out, as in the case of trypanosomes, it seems probable that glutathione or some other sulfhydryl compounds of the tissues might react with arsenoxide, and this, of course, would reduce the amount of such compounds in the tissues to such an extent that they would be injured In our study the low sulfur content of the skin of patients with arsphenamine dermatitis gave the lowest values obtained in the entire study This low sulfur content is doubtless the result of demands made on the organism for sulfur, which Voegtlin and his co-workers have shown plays an important rôle as a detoxifying agent in arsenical poisoning

It is interesting to note that in Voegtlin, Dyer and Leonard's study sodium thiosulfate failed to show a detoxifying power for arsenoxide as did the sulfhydryl compounds tested, especially reduced glutathione They failed, therefore, to offer an experimental explanation of the common use of sodium thiosulfate in the treatment of arsenical poisoning They suggested that intravenous injections of glutathione be employed Since glutathione is difficult to obtain, Voegtlin, Dyer and Leonard thought that it might be possible to secure a beneficial effect by increasing the cystine-glutamic acid content of the patient's diet, since the toxicity of arsenic was reduced if the animal was fed a mixture of glutamic acid and cystine¹⁸

17 Voegtlin, C, and Thompson, J V Quantitative Studies in Chemotherapy VI Rate of Excretion of Arsenicals a Factor Governing Toxicity and Parasitocidal Action, *J Pharmacol & Exper Therap* 20 85, 1922

18 These experiments suggest that proteins should not be withheld in the treatment of patients with toxicologic reactions to arsenic In such patients and also in those with toxicologic reactions to gold compounds, we administer, in addition to sodium thiosulfate, 10 Gm of glutamic acid daily and cystine, which may be obtained by the free ingestion of yolk of eggs Cystine can be administered cheaply as hydrolyzed wool, which contains 15 Gm per thirty-two cubic centimeters Our studies^{1a} suggest that cystine in hydrolyzed wool is in the form of laevo-cystine

In experiments on toxicity in rats, Voegtlin, Johnson and Dyer¹⁹ demonstrated that cystine, cysteine and glutathione detoxified cyanide, sodium thiosulfate and thioglycolic acid also offered protection. They expressed the belief that cyanide reacts chemically with the cystine and glutathione of the body and that detoxification can essentially be attributed to the restoration of the proper physiologic concentration of these compounds in the tissues by the addition of an extra supply of sulfur from without.

From the foregoing data and in view of our findings of a low percentage of sulfur in the skin and nails of persons with systemic infections and disorders it appears that the skin acts as a depot of sulfur on which demands are made as part of the defensive mechanism operative in infections and intoxications. Apparently sulfur in organic combination, especially compounds containing the sulfhydryl radical or divalent sulfur, act as detoxifying agents, although there is evidence that sulfur compounds not existing normally in the organism, sodium thiosulfate for example, may furnish sulfur in an active form.

Voegtlin, Dyer and Leonard's employment of sulfhydryl compounds and their suggestions as to diet are pertinent in the treatment of other intoxications and of systemic infections.

It is possible that determination of the sulfur content of the skin or, what is more practical, of the nails, if it is shown that the percentage of sulfur in the nails correlates that in the skin, may be of practical value in the study of some systemic infections, intoxications, cutaneous diseases and pathologic states and may furnish clues as to sulfur therapy.

TOTAL SULFUR CONTENT OF THE SKIN OF PATIENTS WITH VARIOUS DISEASES OF THE SKIN

A total of thirty-nine examinations were made of the sulfur content of the skin or scales or both of thirty-three patients with disease of the skin, eleven different diseases being represented.

It was observed that the percentage of sulfur in scales from skin in which the percentage of sulfur was normal (from 0.25 to 0.30) ranged from about 0.68 to about 0.80. The percentage of sulfur in scales varied from two and one-half to two and three-fourths the amount contained in the skin. The percentage of sulfur in the skin can therefore be approximated from the percentage in the scales.

The sulfur content was within normal limits in the skin of from one to three patients with the following diseases: generalized eczema, syphilis (secondary stage), lichen planus, pemphigus (estimated from scales), diffuse seborrheic dermatitis (psoriasisiform type), sycosis vulgaris and pyoderma and of eight patients with dermatitis exfoliativa. The percentage of sulfur was low (0.22) in one patient with lupus vulgaris and low normal in one patient with sarcoid of

¹⁹ Voegtlin, C., Johnson, J. M., and Dyer, H. A. Biological Significance of Cystine and Glutathione. I. On the Mechanism of the Cyanide Action, *J. Pharmacol. & Exper. Therap.* 27:465, 1926.

Boeck with pulmonary tuberculosis, it was normal in another patient with the same disease with pulmonary involvement. In two patients with disseminated neurodermatid (prurigo of Besnier) the percentage of sulfur was high (0.34 and 0.45 at the age of about 20). Of seven adults with lupus erythematosus the percentage of sulfur was definitely high (0.35, 0.36, 0.40 and 0.47) in four, it was normal in two and low in the remaining one.

Comment—The tendency for the sulfur content to be low in the skin of patients with lupus vulgaris and sarcoid of Boeck is in accordance with our observations of a low percentage of sulfur in the skin and nails of patients with pulmonary tuberculosis.

The presence of a high percentage of sulfur in four of six patients with lupus erythematosus is consistent with the results of the studies of Crosti,⁷ in which it was observed that the amount of glutathione was increased in the skin of one patient with lupus erythematosus. It is difficult to interpret the significance of these observations. They are in contrast to the presence of a low percentage of sulfur in patients with pulmonary tuberculosis and to the tendency for low values in patients with chronic systemic infections.

Ward²⁰ and others have shown that cystine is the only aliphatic amino-acid of the protein complex which has any marked absorption for solar ultraviolet rays. The capacity of cystine to absorb solar ultraviolet rays is much greater than that of any of the known aliphatic compounds. This power is as great for lesser wavelengths as that of phenylaminopropionic acid, which has the cyclic phenyl group in its molecule. It appears, therefore, that the protective action of keratin-containing tissue against ultraviolet rays is due to its cystine complexes.

In a previous study,^{1b} we therefore determined the sulfur (cystine) content of the nails of four patients sensitized to the sun. The results were negative, the percentage of sulfur was normal.

It is to be noted that the percentage of sulfur, as presently discussed, is uniformly high in the skin of patients with psoriasis, which disease is benefited by exposure to the sun, whereas the percentage of sulfur is high in lupus erythematosus, which disease is adversely affected by sunlight, the percentage tends to be low in pellagra, which disease is likewise adversely affected by sunlight. From these data it does not appear that sulfur metabolism of the skin is concerned in the pathogenesis of sensitization to the sun.

Although further studies are being conducted on the percentage of sulfur in the skin of patients with chronic pyogenic infections of the skin, it is interesting to note that the percentage of sulfur was normal in two patients with sycosis vulgaris and in one patient with chronic

²⁰ Ward, F. W. The Possible Ring Structure of Cystine, *Biochem J* **17** 898, 1923.

pyoderma. These normal findings offer no explanation for a lack of the defensive rôle that sulfur may play in the pathogenesis of chronic pyogenic infections of the skin. The findings are in contrast to the tendency toward low sulfur values in the skin of patients with systemic infections.

PERCENTAGE OF SULFUR IN THE SKIN OF PATIENTS WITH PSORIASIS

Thirty-two patients with psoriasis were examined. A total of forty analyses was made of the percentage of sulfur in the scales, the uninvolved skin of the

TABLE 2—*Percentage of Sulfur in the Skin at the Site of Psoriasis, in the Uninvolved Skin of Patients with Psoriasis and in the Skin After Disappearance of Psoriasis*

Case	Sex	Age	Stage of Disease	Duration, Years	Percentage of Sulfur		
					Uninvolved Skin	Involved Skin	Skin After Disappearance of Psoriasis
1	F	46	Acute, generalized	20	.	0.52	
2	M	26	Acute, severe, generalized	10		0.44, 0.53*	0.34
3	F	48	Scattered patches on extremities	40	0.36	0.38	0.39†
4	F	73	Chronic, few patches	20		0.49	
5	M	71	Chronic, few patches	10	0.39		
6	M	42	Acute, many patches	15		0.38	0.33
7	F	53	Chronic, scattered patches	6	0.39	0.50	
8	M	29	Chronic, scattered patches	6	0.39	0.44	
9	M	34	Acute, many patches	10	0.45	0.48	
10	M	42	Subacute, many patches		0.37		0.34
11	F	46	Chronic, few patches	20		0.42	
12	F	65	Chronic, few patches	2	0.34		.
13	M	40	Acute, many patches	18	0.36		
14	M	54	Acute, generalized	20			0.39
15	M	66	Chronic, patches on legs and scalp	20			0.43
16	M	38	Few mild lesions on trunk	7			0.37
17	M	67	Inactive, mild, scattered patches	21		0.44‡	0.46
18	M	54	Acute, generalized	20			0.39
19	F	40	Acute, generalized	20		0.45	
20	M	53	Chronic, few lesions	13	0.33§		
21	M	64	Chronic, scattered patches	27		0.34	
22	F	35	Chronic, scattered patches	10		0.38	
23	M	21	Chronic, scalp	2			0.33

* Percentage of sulfur after eighteen injections of liver extract

† Percentage of sulfur after twelve injections of liver extract

‡ Percentage of sulfur on a diet low in protein

§ The patient had arthritis, the percentage of sulfur in the nails was 2.39

patients with psoriasis, the skin at the site of psoriasis or the skin after the disappearance of the disease. A combination of these examinations was made on some of the patients. The ages of the patients ranged from 10 to 71 years.

In all cases except two an abnormally high percentage of sulfur was present in uninvolved skin, in skin involved by psoriasis and in skin after the disappearance of the disease. In the two exceptions the percentage of sulfur in the uninvolved skin of one patient was 0.28 (normal) and in the uninvolved skin of another patient, 0.31 (high normal). The data for these patients are omitted from table 2.

Generally it was observed that the skin at the site of psoriasis contained a greater percentage of sulfur than the uninvolved skin and that after the disappearance of the disease the percentage of sulfur decreased to an amount approximating that found in the uninvolved skin during psoriasis (see table 2). For example, the average percentage of sulfur in the uninvolved skin of eight adults with psoriasis was 0.37, whereas in the skin of eight patients at the site of psoriasis it was 0.44 and in the skin of eight patients after the disappearance of psoriasis it was 0.38. For comparison, we regard the normal range of the percentage of sulfur in the skin of adults to be from 0.25 to 0.30.

The highest percentages of sulfur in the group of specimens from patients with psoriasis, indeed, in all specimens in the entire study, were present in the uninvolved skin of two children. The percentage of sulfur in one child, aged 10 years, was 0.71, and in the other, aged 15 years, 0.56. The data on these patients are omitted in table 2. These high percentages can doubtless be correlated with the age of the patients. As stated previously, the normal range of percentage of sulfur in the skin of children is higher than that in the skin of adults. In one other child, aged 10 years (from the group of patients with psoriasis), the percentage of sulfur in the uninvolved skin was 0.42, which is low in comparison with that found in the skin of the other two children. This child was the only patient in the group with psoriasis who had an associated pyoderma. It is to be noted that many writers have commented on the rarity of pyogenic infections of the skin in patients with psoriasis. The high percentage of sulfur in the skin of patients with psoriasis should be considered in explanation of the infrequent association of pyoderma and psoriasis.

The patients in cases 2 and 3 (table 2) were treated with injections of liver extract, such injections being without apparent effect. In one patient the skin (psoriasis still present) showed a greater percentage of sulfur after than before the injections of liver extract. In the other patient the percentage of sulfur was the same before and after the liver therapy. The second examination of this patient was made after the disappearance of the psoriasis, which was treated locally.

One patient in the series had arthritis. The uninvolved skin showed a percentage of sulfur of 0.33, which is low in comparison with the percentage found in other patients with psoriasis. The nails of this patient likewise showed a low percentage of sulfur, namely 2.39.

The percentage of sulfur in the scales of patients with psoriasis ranged from 0.78 to over 0.90. These figures are consistent with the high percentage of sulfur in the skin of patients with psoriasis.

Acuteness or chronicity of psoriasis and its resistance to treatment could not be correlated with the percentage of sulfur in the skin. In only a few patients was a high percentage of sulfur (above 0.50) in the skin associated with severity of the disease and its resistance to treatment.

Comment—Other investigators have reported a high percentage of sulfur in psoriatic scales. Krakow²¹ found a percentage of 1.88 as compared with 0.74 in the normal skin of the palm. In Strickler and Adams'²² analysis of seven specimens the percentage ranged from 0.82

²¹ Krakow, cited by Joffe³⁰

²² Strickler, A., and Adams, P. D. The Nitrogen and Sulphur Content of Scales in Psoriasis and Exfoliative Dermatitis, *Arch Dermat & Syph* 25:11 (Jan) 1932.

to 0.95 in six, in the remaining one it was 0.74 Gruneberg²³ reported a high sulfur content in psoriatic scales

We are not acquainted with any reported study of the percentage of sulfur in the skin of a large number of patients with psoriasis Gruneberg reported an analysis of the percentage of sulfur in the skin of four patients with psoriasis In four of five specimens the percentage of sulfur was high, ranging from 0.38 to 0.53 The highest values were obtained in the skin at the site of healing lesions Gruneberg did not study the skin after the disappearance of the disease He presumed that the percentage of sulfur is high in the latent stage of psoriasis since it is high in the healing stage Gruneberg attributed a high sulfur content in the skin of persons with psoriasis to a possible alteration in the function of the cortex of the adrenal gland One gathers from Gruneberg's report that the therapeutics of psoriasis should be directed toward increasing the sulfur content of the skin Apparently for this reason Gruneberg treated persons with psoriasis with extract of the adrenal gland, since Kubo has shown that such administration increased the sulfur content of the skin of rats and rabbits He also employed liver therapy,²⁴ since Milbradt has shown that administration of liver extract causes an increase of glutathione in the skin

Our study in which it was observed that the percentage of sulfur in the skin tends to decrease after the disappearance of the disease, yet is still abnormally high, would suggest that the therapeutics of psoriasis should be directed toward decreasing the high percentage of sulfur

An abnormally high percentage of sulfur in the skin of patients with psoriasis suggests that the metabolism of sulfur is abnormal There is reported evidence of disturbance of sulfur metabolism in psoriasis, some of which, however, is conflicting Hammerli²⁵ found an increase in the excretion of sulfur, which Geber²⁶ could not corroborate in his study Danilevskaja,²⁷ as well as Levin and Kahn,²⁸ found an increase in

23 Gruneberg, T Mikroanalytische Untersuchungen über den Schwefelgehalt normaler und krankhaft veränderter Haut unter besonderer Berücksichtigung der Psoriasis, *Arch f Dermat u Syph* 168:183, 1933

24 Gruneberg, T Die Lebertherapie der Psoriasis, *Dermat Wchnschr* 97 1793, 1933

25 Hammerli, T Untersuchungen über den mineralischen Stoffwechsel bei Psoriasis, *Monatsh f prakt Dermat* 53:177, 1911

26 Geber, H Nitrogen und Schwefelstoffwechseluntersuchungen bei Psoriasis vulgaris, *Dermat Ztschr* 20 377, 1913

27 Danilevskaja, E Anorganischer Schwefel im Blut und Schweiß der Hautkranken, *Russk vestnik dermat* 7 690, 1929

28 Levin, O L, and Kahn, M The Chemistry of the Body in Diseases of the Skin, *Am J M Sc* 162 698, 1921

the nonprotein sulfur content of the blood, and Gallego Burin²⁹ and others reported a decrease in the glutathione content of the blood. Joffe³⁰ observed a decrease in the sulfate content of the urine, which increased after improvement of the disease. In an interpretation of high percentage of sulfur in the skin of patients with psoriasis the following considerations are perhaps pertinent. Sulfur compounds, especially glutathione, are essential physiologic tissue constituents concerned in biologic oxidation-reduction phenomena. There is evidence that the pathogenesis of psoriasis concerns the oxidation-reduction mechanism of the epithelial cell, a view championed by Van Kerkhoff³¹.

On the basis of our findings we favor the use of a diet with a low protein content in therapy for psoriasis, as advocated by Schamberg, but do not find liver therapy of value. It is difficult to correlate our findings with the beneficial effects of a diet poor in fat and evidence of a disturbance of fat metabolism in psoriasis, as reported by Grutz and Burger³².

SUMMARY

The total sulfur content of the skin was determined according to the method of Frear and is expressed as percentage of sulfur.

The sulfur content of the skin was determined from the following sources: (1) the skin of man from infancy to old age, (2) the skin of rabbits from birth to maturity, (3) the scales and skin of patients with various cutaneous diseases, especially psoriasis, (4) the skin obtained at autopsy on patients with systemic infections or disorders, and (5) slowly and rapidly growing carcinoma in mice and malignant lesions in man.

Sulfur in the skin exists essentially in organic combination. It is believed that a large portion is in the form of cystine and cysteine.

The sulfur content of the skin decreases with age both in rabbits and in man. The normal percentage of sulfur in the skin of infants ranges from 0.40 to 0.50, it decreases the first few years of life to about 0.35, at adolescence it is about 0.30 per cent, and in adults it ranges from 0.25 to 0.30 per cent.

The rate of growth of mouse carcinoma correlated the sulfur content. The sulfur content of benign (nonhairy) melanoma of the skin

29 Gallego Burin, M. Glutathion y psoriasis, *Actas dermo-sif* 26 373 (Feb) 1934.

30 Joffe, M. Sulphate Metabolism in Psoriasis, *Urol & Cutan Rev* 38 261, 1934.

31 Van Kerkhoff, J. H. P. Beiträge zur Kenntnis der Psoriasis vulgaris und ihrer Behandlung, Leipzig, S. Hirzel, 1929.

32 Grutz, O., and Burger, M. Die Psoriasis als Stoffwechselproblem, *Klin Wchnschr* 12 373, 1933.

was generally high. Malignant melanomas of the skin contained a still greater percentage of sulfur. The sulfur content of malignant tissue from various viscera did not show uniformly a greater percentage of sulfur than that contained in the organ from which malignant growth arose.

The sulfur content of the skin was low and low normal in one half of the series of patients dying of acute and chronic infections and in the majority of patients dying of tuberculosis. The sulfur content of the skin of persons with pellagra was low and low normal. It was uniformly low in the skin of patients with arsphenamine dermatitis.

The sulfur content of scales varied from two and one-half to two and three-fourths the amount contained in the skin.

Of twelve different cutaneous diseases in which the sulfur content of the skin was examined, there was a tendency toward a low value in lupus vulgaris and sarcoid of Boeck, the content was high in four of seven patients with lupus erythematosus and uniformly high in patients with psoriasis. The percentage of sulfur was abnormally high in the skin at the site of psoriasis, in the uninvolved skin and in the skin after the disappearance of the disease. As a rule the skin at the site of psoriasis contained a greater percentage of sulfur than the uninvolved skin, and after the disappearance of the disease the percentage of sulfur decreased, approximating that of the uninvolved skin during psoriasis.

The significance of these findings is discussed with reference to the rôle that sulfhydryl compounds play in cellular activity of normal and abnormal growth and the rôle that sulfur plays in the defensive mechanism. It appears that the skin acts as a depot of sulfur on which demands are made in infections and intoxications. The evidence of altered metabolism of sulfur in psoriasis is also considered.

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TRYPARSAMIDE

A FURTHER QUESTIONING OF THE ALLEGED NONSPIROCHETICIDAL PROPERTIES OF THE PENTAVALENT ARSENICAL IN TREATMENT OF HUMAN SYPHILIS, WITH A SUGGESTION REGARDING ITS READOPTION INTO THE CURRICULUM OF THERAPY FOR EARLY SYPHILIS

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The pentavalent arsenical compound tryparsamide, as synthesized by Jacobs and Heidelberger, was produced at the Rockefeller Institute in 1917. It possesses the following structure: the sodium salt of normo-phenylglycinamide-para-arsenic acid, containing 25.32 per cent arsenic in pentavalent form. It is a white crystalline powder, colorless and odorless in water, in which it is readily soluble. Early experimental inquiry demonstrated that the tolerance of different animal species for it varied widely, that the toxic effects were confined to doses close to the minimal lethal dose, which was distinctly high, and that recovery from a sublethal dose was peculiarly rapid and complete. Several persons reported most favorable results from its use in treatment of trypanosomiasis in man. This work was followed by a report in 1919 by Brown and Pearce, who studied a large series of animals that were infected with various strains of trypanosomes and spirochetes. They noticed that there was no organic or functional disturbance following the administration of a therapeutic dose of tryparsamide and that although the action of the drug in treatment of spirochetal infection was not striking, "a very definite effect is produced upon the course of the infection by *Treponema pallidum*. In the case of blood spirochetes the infection is ameliorated and even though the spirochetes are not immediately destroyed the infection is frequently brought to a termination which leaves the animal in a condition not unlike that produced by more powerful spirocheticidal agents. It does possess a considerable degree of spirocheticidal action, but its chief effect is seen in the peculiar manner in which it modifies or controls the course of the infection."

A further report by Lorenz, Lovenhart, Bleckwenn and Hodges was most enthusiastic regarding the use of tryparsamide in treatment of neurosyphilis. They stated that the use of this drug in therapy of syphilis was based not on its spirocheticidal action, which is comparatively feeble, but on its unusual features: the promptness of recovery of an experimental animal from toxic injury following the use of the drug, the tolerance of the subject to repeated doses of the drug, its

decided tonic effect and its ability to induce resolution and healing of syphilitic lesions, even in the presence of actively motile spirochetes. A clinical study published by Moore, Robinson and Keidel stated that they had used tryparsamide in treatment of the various types of syphilis occurring in man. From their results in treating eight patients with early syphilis, one of whom had primary involvement, they concluded that the drug is contraindicated at this stage of the disease because of its feeble spirocheticidal activity. In twenty-four cases of late syphilis they found therapy with tryparsamide to be inferior to therapy with arsphenamine and stated that it should be used to supplement treatment with mercury and arsphenamine, not to supplant it. A later report by Moore, Robinson and Lyman, dated Sept 20, 1924, gave conclusions based on the treatment of one hundred and thirty-three patients with neurosyphilis. They stated that in primary and secondary syphilis or in tertiary syphilis unaccompanied by neurosyphilis, the improvement after tryparsamide therapy was so slight that its further use in treatment of these infections was precluded. In this group ten cases of "primary and secondary syphilis" were cited in which the dose of tryparsamide was as high as 7 Gm but failed to heal the lesions. No indication of the number of cases of primary syphilis was given. It was also stated that the most striking clinical results were obtained from treating patients with meningovascular involvement. Pearce and Brown¹ intimated that their results were similar to but more favorable than those of Moore and his associates. Healing of lesions was hastened by tryparsamide therapy, and the Wassermann reaction of the blood became almost negative. They treated "a few patients showing indolent or regressive primary and secondary lesions with distinctly favorable effect. A few patients with active primary or secondary lesions were subsequently treated. The lesions were unaffected or the activity so increased that the drug was discontinued." No definite statement was made regarding the number of cases in this series. Neither was mention made of the number of primary lesions treated. As a result of these early findings, work on the effect of tryparsamide therapy in man was confined almost exclusively to the action of the drug in the treatment of neurosyphilis. One somewhat divergent and later observation by Futaki is of interest. He noted that in a case of rat bite fever in man due to *Spirochaeta morsus-muris*, the primary sore healed as rapidly with the use of tryparsamide as with the use of arsphenamine. On the other hand, there was little or no effect on other secondary cutaneous lesions and no beneficial action on the course of fever. Solomon, Epstein and Buike suggested that there were stimulation and healing of local tissue from the use of tryparsamide without

1 Pearce, L., and Brown, W. H. New York State J. Med. 24 751, 1924

destruction of the blood-borne spirochetes. A great deal of animal experimentation with this drug concerning the following factors has been performed: the minimum lethal dose, the arsenic content of blood following its use, the mode of its excretion and its ability to penetrate into the spinal canal. To a lesser degree the latter three phases have been studied in relation to the effect of the drug in treatment of human beings. As is typical of research on syphilis, opposite opinions were voiced. For instance, Voegtlin, Smith, Dyer and Thompson demonstrated that tryparsamide possesses to a high degree the ability to penetrate into the central nervous system, on the other hand, Fordyce and Meyers stated that tryparsamide does not possess unusual penetrative power. The history of tryparsamide is interesting, and the drug holds an enviable position in the present armamentarium against syphilis. At the outset, however, it was subjected to no small degree of criticism, and it suffered the vicissitudes common to so many new compounds recommended for use in the therapy of syphilis. It appears that the early pessimism accorded the action of the drug, including its use solely in the therapy of neurosyphilis, was due to observations made over too short a time. As the years passed, the judgment became more favorable, until today tryparsamide is considered by many authorities to be equal to malaria therapy for the treatment of neurosyphilis. It is true that the production of toxic amblyopia in a relatively small proportion of patients treated with tryparsamide has been of sufficient moment again to cause the value of this drug to be questioned. It is interesting that while some observers stated the belief that involvement of the optic nerve does not obtain in animals following the use of tryparsamide, more recently Young and Lovenhart demonstrated that the toxic effect of the arsenicals on the optic nerve is distinctly related to the molecular structure of the compounds and that arsenicals with the amino group in a para position to the arsenic, such as atoxyl and tryparsamide, produce optic lesions in rabbits, while arsenicals with the amino group in a meta or ortho position to the arsenic, such as arsphenamine or neoarsphenamine, are totally harmless. Without doubt tryparsamide is the safest of the arsenicals to use in the absence of an involvement of the eye-grounds. The presence of this condition may be accurately determined before instituting therapy by an examination of the eyes and a check of the visual fields. The objectionable reactions which may occur from the use of tryparsamide when certain precautions are not taken do not usually obtain until four or five injections have been given, the consensus indicates that after an unfavorable reaction has occurred the patient should not again be subjected to the drug, even after a rest cure.

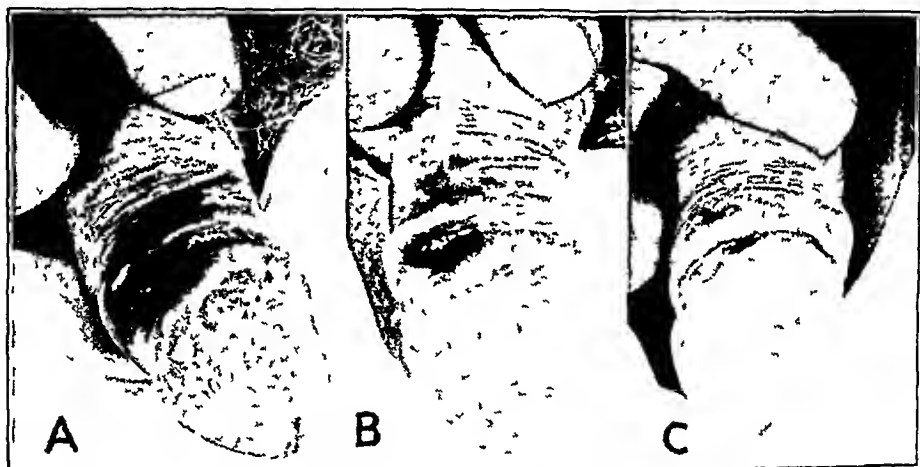
With the exception of the comparatively few instances of toxic amblyopia that have occurred from the use of tryparsamide, objectionable immediate and late reactions common to the other arsenicals are

absent This fact, as well as its action in general, is decidedly paradoxical and difficult to understand when it is remembered that the arsenical content of the average dose is high, being approximately from 240 to 700 mg It should be recognized that beyond the assumption that the drug is a "stimulator of resistance" and a "penetrator of nerve tissue" the mechanism of its action is unknown One must accept the evidence that whereas the use of tryparsamide in the treatment of primary, secondary and tertiary syphilis other than involvement of the nervous system is followed by somewhat mediocre results, its use in the therapy of neurosyphilis has given results far superior to those produced by any other drug that is employed in the treatment of this condition

Although the older experimenters found that the use of tryparsamide in the treatment of early syphilis was unwarranted because it affected only a few lesions and fresh lesions often appeared in spite of heavy doses, not one denied that the drug had some spirocheticidal activity Today, however, the contention is common that tryparsamide possesses no spirocheticidal properties and that therefore its use in the therapy of neurosyphilis should be supplemented by the use of arsenicals possessing spirocheticidal properties This statement is made despite the fact that many experienced earlier reporters contended that they obtained better results in treating neurosyphilis with tryparsamide alone than with it in combination with other metals For these reasons and because of the paucity of research on the action of tryparsamide on primary syphilis and, also, because I believed that the contention that the drug totally lacks spirocheticidal properties is neither scientific nor justified in the light of former experience, I used tryparsamide again in treating primary syphilis Those who declaim this procedure as unnecessary because of the vast amount of animal research performed with tryparsamide must recognize that while the results of animal experimentation are usually helpful, they are not applicable in the strictest sense to man Most animal experimentation with a drug is based on determining the curative dose, i e., that single dose which will neutralize a recent infection in an animal The status of cure is judged by the healing of lesions, the disappearance of spirochetes or the fact that negative results follow the transplanting of a gland from the infected animal to a healthy one In treating the disease in man, it is impossible to administer a single curative dose of any drug The major toxic reactions common to man do not occur in animals, furthermore, certain physiologic reactions differ widely in animals and in man, for example, the best therapeutic index for arsphenamine in animals is from 1 to 12, and the best for neoarsphenamine is 1 to 25, these values indicate that the action of neoarsphenamine is superior to that of arsphenamine, whereas for man the preponderance of evidence indicates that the reverse obtains

The first case observed was that of a patient with a chancre of approximately four days' duration. He had received no local medication. The intravenous injection of 2 Gm of tryparsamide was followed by no visible manifestation of healing. Twenty-four hours after therapy, a slight enlargement of the lesion occurred, not a Herxheimer reaction but merely the advance in the cycle which one might expect without therapy at this stage. Dark-field examination revealed living spirochetes. I instituted neoarsphenamine therapy and used a smaller dose than usual at first because of the pentavalent arsenic already given. This early change of therapy was made because I am mindful of and fully concur with Pusey's dictum concerning the golden value of the early therapeutic hours.

The second case came to my attention more recently. A young man of approximately 24 years of age presented a chancre of about three weeks' duration. Local medication had been used but had been discontinued in disgust four days previously, as the lesion steadily became worse. Examination by dark field gave positive results, the Wassermann test of the blood showed a 3 plus reaction, there was localized adenitis but no sore throat, headache or rash. Figure A was taken on



A, photograph taken on Sept 17, 1935, before treatment was instituted. B, photograph taken on September 19, forty-eight hours after 2 Gm of tryparsamide had been administered. C, photograph taken on September 23, six days after therapy with tryparsamide was started.

Sept 17, 1935. The patient was given 2 Gm of tryparsamide intravenously, on the next day there was definite evidence of healing and only a slight manifestation of a localized reaction of the Herxheimer type. Approximately twenty-four hours after institution of tryparsamide therapy systematic dark-field search of many fields revealed only 2 spirochetes. Forty-eight hours after therapy was started, no spirochetes could be noted in numerous searches. Figure B was taken on Sept 19, 1935. On September 21 3 Gm of tryparsamide was given. Figure C, taken two days later, on Sept 23, 1935, illustrates the degree of clinical change that occurred six days after the institution of tryparsamide therapy. The chancre was entirely healed ten days after the first dose of tryparsamide.

It becomes evident that in some cases and under certain conditions tryparsamide is definitely spirocheticidal in man. It is interesting that this small series of cases corroborates the former observations of Pearce,

who found that an early chancre was unaffected or even aggravated by tryparsamide therapy while healing of an older chancre was definitely stimulated by its use. I should like to emphasize the fact that although the evidence of repair shown in figure *B*, taken forty-eight hours after the institution of tryparsamide therapy, is perfectly clear, it does little justice to the physical change observed. Indeed, the evidence of immediate healing was equaled only by the numerical reduction and diminished activity of the remaining spirochetes. Experiments were conducted to determine the action of tryparsamide on the living, shortly isolated, spirochete. Fields were obtained showing many motile spirochetes, a dilution of tryparsamide equal to the average hematogenous dilution in the human being was made. This was allowed to permeate the fields by capillarity. The organisms ceased all movement within a few minutes, many of them showing distorted angulation. These tests proved to be entirely useless, as the use of physiologic solution of sodium chloride or even sterile water caused the same phenomena, i. e., the early loss of motility of the spirochetes and their distortion. Perhaps the sudden alteration of temperature or of concentration may be the occasioning factor, but no conclusion has yet been reached regarding these peculiar reactions.

It may be stated that the contention that tryparsamide lacks spirocheticidal properties is without foundation in fact, and the assertion that better results are obtained in the treatment of neurosyphilis when tryparsamide is supplemented by other arsenicals cannot yet be universally accepted as statements to the contrary have been made by several persons of unquestioned experience. Furthermore, it cannot be denied that there is difficulty in understanding why a drug like neoarsphenamine, which fails over an adequate period to check the degenerative clinical phenomena of neurosyphilis even when supported by various other metal compounds should suddenly acquire merit when used in conjunction with an arsenical of different structure. Were the condition that of an alternate metallic action an explanation might be acceptable on the basis of the habituation of the organism to a drug, but it seems that one is deprived of that reasoning here, since two arsenicals are being dealt with, and the suggestion of symbiotic action is somewhat unique outside the realm of the micro-organism. Furthermore, if tryparsamide is deprived of all spirocheticidal properties, how can one adequately explain the distinct beneficial clinical results following its singular use in meningovascular syphilis, a condition which can be legitimately classified only as an acute infectious process or the exacerbation due to intense activity of the spirochete? It is commonly admitted that this is the type of neurosyphilis most amenable to therapy with tryparsamide. The purpose of this paper, however, is not only to question the spirocheticidal properties of tryparsamide but largely to

advocate its use as part of the routine treatment of early syphilis. It is generally admitted by the foremost authorities that with the present mode of therapy from 18 to 20 per cent of the patients are modestly labeled as having "inescapable breakdowns", in other words, they are patients destroyed by the disease, of these, 12 per cent have neurosyphilis. This condition develops in spite of the excellent modern standards of syphilotherapy. It is an accepted fact that von Jauregg, using malaria therapy, demonstrated that many of the persons with neurosyphilis could be reclaimed after having reached a condition of actual degeneration. Other workers, over a period of time, stated that tryparsamide gave equally good results in the process of reclamation. It must be further recognized that certain primary lesions may flourish in the face of either form of therapy. Thus, it will be noted that a close parallel exists between the clinical results obtained by the use either of malaria or of tryparsamide. Is it therefore not logical to believe that a similar parallel exists after the use of either of these agents in the early therapy of syphilis?

Kyrle² stated the premise that if malaria was possessed of such beneficial qualities as to be able to reclaim many of those suffering actual degeneration from the ravages of the disease, its action previous to any destruction of the central nervous system should be of far greater benefit. In other words, it should possess the property of prophylaxis. How his perspicacity was rewarded may be gleaned from the report of Matuschka and Rosner, made after his death, five or six years after the institution of his method. The report concerned treatment of two hundred and thirty-two patients and is worthy of recapitulation. The severity of the test is understood only when one recognizes that a single course of treatment was given to each patient. This single course consisted of arsphenamine, malaria and arsphenamine.

Duration of Disease From 1 to 2 years	Reaction of Blood to Wassermann Test Before Treatment Positive 232	Reaction of Blood to Wassermann Test After Treatment		
		Negative 230	Influenced 99.1%	Uninfluenced 0.9%

In fifty-six of the cases in which the reaction of the spinal fluid had been positive, it became negative. Tests of the blood and of the spinal fluid of the patients continued to give negative results, and the patients showed no clinical evidence of syphilis for five years.

The essential value of this group of cases becomes evident only when it is realized that most early reports on the therapy of syphilis embracing thousands of cases have usually dwindled to a number rarely in excess of that in the series just cited at the end of five years, which is the minimum period of value for judging a cure.

2 Personal communication at the Finger Clinic in Vienna, 1925

Because of the profound difficulties of administering malaria therapy in the early stages of the disease, with its enforced incapacitation for a longer or shorter time, the main reaction to the foregoing report has been a feverish indulgence in utilizing various methods other than malaria for elevating the temperature of the body, in spite of the fact that von Jauregg, who had had some twenty-five years of previous experience with elevation of body temperature by various methods in the therapy of syphilis, sounded a pessimistic note at the outset, which has apparently been sustained. He persisted in maintaining that biologic reactions other than the effect of raised body heat enter into the reaction equation, which is imperfectly understood.

The success of Kyrle's procedure suggested further evidence in support of the contention that two separate and distinct types of spirochetes exist in the production of the disease. One type is resistant to forms of treatment other than malaria or tryparsamide. Irrespective of theories, it cannot be denied that the utilization of modern continuous alternate metallic therapy in early syphilis has proved inadequate in controlling the condition of 20 per cent of all patients so treated, while early malaria therapy supported by metals has demonstrated beyond question its effectiveness. Because of the difficulty of giving malaria therapy to patients with early stages of syphilis and because a close parallel obtains between the clinical results of therapy with malaria and those of tryparsamide therapy in patients with late degenerative syphilis, I have incorporated tryparsamide into my curriculum of therapy for early syphilis. In other respects the course of treatment closely follows the outline of continuous alternate metallic therapy as given recently by the Cooperative Clinical Group, I shall report on these cases in the future.

SUMMARY

In some instances tryparsamide possesses definite spirocheticidal properties.

The present generally adopted methods of metallic therapy result in the loss of about 20 per cent of the patients treated.

The method of Kyrle, in which malaria is utilized prophylactically in treatment of early syphilis, renders the maximum of good results, that is, 99 per cent of the patients are cured.

As malaria therapy is largely proscribed in the early stages of syphilis for many obvious reasons, the suggestion is made that tryparsamide be incorporated into the regular curriculum of metallic therapy of early syphilis, irrespective of its apparently mediocre value in suppressing early lesions, because its effect so closely parallels that of malaria in the clinical end-results in the therapy of neurosyphilis.

HALO NEVUS

LEUKODERMA CENTRIFUGUM ACQUISITUM (SUTTON),
LEUKOPIGMENTARY NEVUS

SAMUEL FELDMAN, M D

AND

ISIDORE M LASHINSKY, M D

NEW YORK

In 1916 Sutton reported two cases of a condition which he considered to be an unusual variety of vitiligo, and he named the disease leukoderma centrifugum acquisitum¹ In one case there was one oval patch, in the exact center of which was a small round elevated brownish maculopapule It resembled a small pigmented nevus and, according to the statement of the patient, had been there only since the onset of the attack, which dated back three years There was no hyperpigmented areola surrounding the patch of vitiligo

The second patient had four lesions which were similar to the one described Two of the lesions were faint and almost imperceptible, the mother of the patient stated that originally one of these patches was much more distinct but that it had gradually regained some of its color

On microscopic examination Sutton noted an increase of pigment in the basal layer of the epidermis in the central zone and an infiltration in the cutis of cells which stained deeply with basic dyes, which he interpreted as being of endothelial origin There was no mention of any change in the white zone

Sutton's interpretation of the condition in his two cases was based on several considerations In spite of the fact that he made no mention of it in his paper, one could surmise that he considered the condition as leukoderma because of the mother's statement that one of the patches had regained some of its normal color One need not emphasize the uselessness of such information for the purpose of making scientific deductions His further deduction that the condition was acquired was evidently made from a statement in the history that the condition was not present at birth Even if this is taken for granted, one is not justified in assuming that this disease is acquired in the sense that one may acquire an infection, because it is known that even true nevi may not

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1 Sutton, R L An Unusual Variety of Vitiligo (Leukoderma Centrifugum Acquisitum), J Cutan Dis 34 797, 1916

appear until later in life. "Centrifugum" in the title was probably meant to indicate a reversal of the so-called *Pigmentverschiebung* so often mentioned in the German literature. It simply expresses changes which occur under certain conditions when the cutaneous pigment disappears or becomes diminished in certain locations and increases in others. In vitiligo this relative increase in pigmentation takes place immediately at the border of the patch. Whether or not the coners of the term *Pigmentverschiebung* actually thought that the pigment is transferred from the depigmented to the pigmented area by some agent is, of course, hard to determine, however, it seems that that is the impression of some dermatologists. In Sutton's disease the pigment is supposed to be deposited in the center of the lesion instead of at the periphery. For that reason Sutton and a number of others who reported similar cases stressed the lack of a hyperpigmented border in that condition. As a matter of fact, pigment is formed in the melanoblasts of the epidermis and is not transferred there. The rôle of the chromatophores is purely passive. They exert a phagocytic action on the pigment which finds its way to the cutis from the melanoblasts. Furthermore, the pigmentation of the center of the lesion in the condition under discussion is true pigmentation and certainly has nothing to do with *Pigmentverschiebung*.

If one takes it for granted that the central spot is a nevus and at the same time assumes that a hyperpigmented border is essential for a diagnosis of either leukoderma or vitiligo, the condition in the cases described by Sutton and others as instances of leukoderma acquisitum cannot be interpreted as either of those mentioned. It would be more reasonable to interpret the achromic patch as a cutaneous defect in the form of local albinism or as achromia associated with other pathologic and functional changes. On the other hand, the lack of a hyperpigmented border is of doubtful value in the interpretation of these lesions, as at least one case has been reported in which a definite hyperpigmented border was present.

REVIEW OF THE LITERATURE

In reviewing the literature on the subject we noted that Hebra and Kaposi² observed the condition as early as 1874. In their textbook of the diseases of the skin, they stated that leukoderma may start near or around a pigmented nevus. In 1910 Sir Humphrey Rolleston³ reported the case of a patient who had obstructive jaundice due to a carcinoma of the mesentery. This patient had round patches of vitiligo, some of which contained a central mole. The vitiliginous portion was

2 Hebra, F., and Kaposi, M. Diseases of the Skin, translated by Warren Tay, London, The New Sydenham Society, 1874, vol. 3, p. 180.

3 Rolleston, H. P. Jaundice, with Area of Unpigmented Skin, Proc. Roy. Soc. Med. (Clin. Sect.) 3: 195, 1910.

jaundiced like the rest of the skin In 1915 Almkvist ⁴ presented a patient who had a pigmented nevus with a white halo, the latter having the characteristics of naevus anemicus In 1917 Shelmire ⁵ reported the case of a man who had numerous white areas, some of which had a centrally located pigmented spot He stated that new lesions were forming which had no pigmented central spots The histologic report was made by J H Black, the same pathologist who reported on the pathologic changes in Sutton's cases That may partly account for the same interpretation of the disease in both instances In describing the changes in the cutis he stated that there were vascular dilatation and a mild infiltration of round cells Deeper than the infiltration were large masses of large ovoid cells which showed prominent and deeply staining nuclei "These cells were apparently endothelial in type" He also stressed the point that there was no hyperpigmentation at the border When one views the photomicrographs appended to both Sutton's and Shelmire's article, one cannot help being impressed by the fact that there is a fair degree of similarity between this pathologic picture and that of pigmented nevus In 1918 Bunch ⁶ presented at a meeting of the Royal Society of Medicine of England a girl 12 years old who had had many patches of vitiligo and two patches of canities on the hairy scalp about one year previously In three of the patches were deeply pigmented moles A biopsy specimen of one of the moles showed masses of cells which had a definite arrangement in bundles and contained pigment These, according to Stogden, who made the biopsy, were probably of endothelial origin Bunch presented two patients with a similar condition, one in 1919 and one in 1920

The year 1920 ended the period during which the central nevus was regarded by some as being made up of endothelial cells Later authors either regarded the central spot as a frank nevus or reported no biopsy

In 1921 Petges ⁷ reported a case in which an ordinary pigmented nevus was surrounded by an area of depigmentation, indistinguishable from vitiligo Nevus cells were found in the pigmented center In

4 Almkvist Ein Fall von eigentümlichen Naevi, *Dermat Wchnschr* **60** 74, 1915

5 Shelmire, J B An Unusual Variety of Vitiligo (*Leukoderma Centrifugum Acquisitum*), *J Cutan Dis* **35** 163 (March) 1917

6 Bunch, J L White Spot Disease and Vitiligo, *Brit J Dermat* **30** 203, 1918, Vitiligo Patches with Central Pigmented Mole, *Proc Roy Soc Med (Sect Dis Child)* **11** 18, 1918, Vitiligo with Central Pigmented Moles, *ibid* (Sect Dermat) **13** 148, 1919-1920

7 Petges Hairy Nevus Surrounded by Vitiligo, *Bull Soc franç de dermat et syph* **6** 302, 1921

the same year Little⁸ reported a case in which there were patches of vitiligo, some of which had a central mole. In 1922 Montpellier⁹ reported one case of his own and reviewed eight from the literature.

The first comprehensive paper on the subject was written by Stokes,¹⁰ in 1923. He stated that he observed more than half a dozen cases in which the center of the lesion was clinically and pathologically a nevus. One patient whose condition he described had previously had many moles without any white-ringed lesions. He later acquired about fifty lesions with white halos about them. He did not say that the halos developed around preexisting lesions, but one gains the impression that that is what he meant to imply. He also reported two cases in which there was achromia around pigmented, verrucous and hairy nevi. He found no pigment in the epithelial cells of the epidermis in the white area and no chromatophores in the cutis, hence there was no phagocytic action to explain the process of depigmentation. Stokes expressed the belief that a physical or chemical disturbance in the equilibrium of the affected skin may be responsible for the destruction of pigment and the disappearance of melanoblasts.

In 1924 Weber¹¹ reported a case in which a central nevus was surrounded by an area of depigmentation. He formulated a law which he called "a law regarding the distribution of depigmented areas when they are superadded to pigmented nevi" and said that when vitiligo of unknown origin occurs in a healthy child, there is a tendency for the vitiligo to surround any mole or nevus that the child may have. That presupposes that in every instance the nevus is the first to appear, the vitiligo being superadded. No one at present would concede the remotest possibility that Weber's postulate might be true, as it is known that nevi without pigmented halos and white patches without central nevi can be found side by side with so-called Sutton's disease in the same patient. Furthermore, it is known that at least in one instance the vitiligo was first to appear, the central nevus developing much later. He presented a girl 8 years old who had patches of typical vitiligo which appeared when she was 7 years old. One of the patches had in its center a miliary raised blackish-brown mole, around which the white patch formed a halo. He asked the question "Is the achromic patch

8 Little, Graham Case Report, Proc Roy Soc Med (Sect Dermat) 14 42, 1921

9 Montpellier Leukoderma Appearing Around Pigment Nevi, Bull Soc franç de dermat et syph 29 81, 1922

10 Stokes, J H Leukoderma Acquisitum Centrifugum (Sutton), Arch Dermat & Syph 7 611 (May) 1923

11 Weber, F P A Law Regarding the Distribution of Depigmented Patches of Vitiligo, When They Are Superadded to Mole-Like Nevi, Brit J Child Dis 21 202 (July-Sept) 1924

also a congenital nevus, the opposite of a pigmented nevus, or is it true vitiligo although limited to a circumscribed area?" We are inclined to answer yes to the first part of the question—that we are dealing with a nevus in the sense of a developmental defect and hope to be able to furnish sufficient evidence to corroborate our belief later on. The fact that in so many of the cases hitherto reported the condition occurred in a child, even to the extent that Weber considered the condition a disease of childhood, should make one think of the probability of the congenital nature of the disease. Weber used a happy expression in describing the condition—that the white patch forms a halo about the black mole. We suggest naming the disease described by Sutton halo nevus.

Narducci¹² reported two cases, in one of which there were several depigmented patches each containing a pigmented nevus. These he called leukopigmentary nevus, another suggestion for an appropriate name. In the other case there were patches of vitiligo, and in only one of them was there a nevus. He thought that in the second case the peculiar arrangement was accidental, and he called it perimevic vitiligo. The skin in the depigmented portion was apparently normal.

In 1924 von Poor¹³ reported a case in which numerous pigmented nevi were surrounded by white areas. There were also pigmented moles without an achromic rim. These were the smallest ones found. He had the impression that the white halo formed only when the mole increased sufficiently in size. The white halo grew in proportion with the increase in size of the pigmented nevus. The patient also observed a gradual increase in the number of lesions. He found islands of pigment in the epithelium of the white area and claimed that the presence of these islands differentiates this disease from vitiligo, in which the depigmentation is complete. His views coincide with those of Stokes, who expressed the belief that the depigmentation is due to a physical or chemical disturbance in tissue balance.

Leszczynsky¹⁴ in his article on Sutton's disease stated that there is a difference in the dopa reaction between this disease and posttraumatic leukoderma. By using the von Groer scale, he found in the normal skin of his patient a value of 16, in the vitiligo-like halos about the nevi a value of 4 and in posttraumatic leukoderma a value of 0. His patient stated that pigmented nevi had been present from birth. There were numerous larger and smaller pigmented nevi which were surrounded by

12 Narducci: Sul neo leucopigmentario et sulla vitiligine perimevica, *Arch ital di dermat, sif* 1: 271, 1925.

13 von Poor, F: Ueber Leukoderma centrifugum acquisitum, *Dermat Wchnschr* 80: 401, 1925.

14 Leszczynsky: Ueber Suttonsche Krankheit, *Dermat Wchnschr* 82: 575, 1926.

a white oval or rounded zone. There were also a number of lesions of molluscum fibrosum with a white halo. In one instance the fibroma itself was depigmented. He stated that the size of the white patch was in exact proportion to that of the nevus, being large when surrounding a large nevus and extremely small when in relation with an almost imperceptible pigmented spot. He observed the simultaneous development of the lesion, starting from a barely perceptible speck to the larger central nevus and its halo. Thus appears to us significant and makes us feel that both are part and parcel of one process. Significant also is the occurrence of the white halo about the fibromas which were present, and as molluscum fibrosum in itself may represent a nevus in the larger sense of the word, we have another variety of the same disease.

Crawford¹⁵ reported the case of a girl who stated that she had had pigmented moles from birth and that the white halos developed recently. This patient also had several patches of vitiligo. Crawford observed an area of hyperpigmentation around one lesion of leukoderma acquisitum.

Krantz¹⁶ reported the case of a patient who had a patch of vitiligo in the center of which there was a hairy pigmented nevus.

Several other cases were reported, but none of them presented any features which might throw light on the subject.

REPORT OF FIVE CASES

CASE 1—Mrs. F. DeS., 36 years old, was a patient in the Morrisania City Hospital, complaining of cardiac disease. When the members of our service were called to see the patient in consultation, there were two white patches, one on the back and the other on the lower part of the abdomen. The lesion on the abdomen was oval, with sharp borders, and measured about $1\frac{1}{2}$ by 2 inches (3.7 by 5 cm) in diameter. The lesion on the back was somewhat larger. The skin was soft and pliable and, aside from its color, appeared in every way normal. In the exact center of each patch was a light brown raised papule. These structures were soft, the surface was somewhat wrinkled, and to all appearances they were pigmented nevi. The size of each nevus bore a direct relation to the size of the white patch.

Pressure with the diascop over the edge of the white area caused a diminution in the contrast in color between that and the normal skin, but the contrast was not entirely eliminated. Striking the area vigorously with the palm caused a reddening of the normal skin, but the white spot remained unaffected. Application of a mustard plaster over one of the patches for fifteen minutes caused a marked erythema of the surrounding normal skin, but the white patch remained unaffected. There was no disturbance in the sense of pain, but the sense of heat and cold was decidedly impaired in the achromic patch. The tactile sense remained intact.

15 Crawford, S. Leukoderma Centrifugum Acquisitum, Arch. Dermat. & Syph. 9:394 (March) 1924.

16 Krantz. Naevus in vitiliginöser Stelle, Zentralbl. f. Haut- u. Geschlechtskr. 16: 872, 1924.

The skin immediately surrounding the white zone showed mild hyperkeratosis, and the granular layer was present but not marked. The stratum Malpighi was normal and consisted of six or seven layers. A moderate amount of melanin was found in the basal cells. The distribution of the pigment was patchy. The corium was normal and made up of loose bundles of connective tissue, poor in cellular elements. In the papillary layer the fibroblasts were more abundant. No hair follicles or sebaceous glands were encountered. The blood vessels were apparently normal.

At the junction of the normal skin with the white patch the epidermis was still normal, but no pigment was seen in the rete. No chromatophores were



Fig 1 (case 1)—Photomicrograph of a section from the central pigmented nevus

noted, but a few scattered free pigment granules were found in the upper layers of the cutis.

In the vitiliginous area, the epidermis was strikingly thin, not more than four or five layers deep and in some places even less. In these locations the papillae were missing and the rete pegs were absent, so that the junction of the cutis and the epidermis was a straight line. The corneal layer was nearly missing and showed some parakeratotic cells. The granular layer was almost absent. In the cutis there was dilatation of the lymphatics and dilatation and engorgement of the capillaries, especially in the subpapillary and upper layers. Some of the engorged capillaries showed perivascular edema, with a minimal amount

of surrounding cellular infiltration, consisting of mononuclear cells. The elastic tissue immediately below the epidermis was fragmented or missing in nearly all areas of the section. It appeared to be diminished in amount in the deeper layers also. Pigment seemed to be entirely lacking in this location.

Near the center of the lesion the rete became more normal in appearance and the papillae and rete pegs became again evident.

In the center of the lesion, the area representing the central pigmented spots, the epithelium was of normal thickness and was thrown into folds. The hyperkeratosis was less marked, but there were a few parakeratotic cells in the section. The granular layer was extremely sparse and for the most part missing.

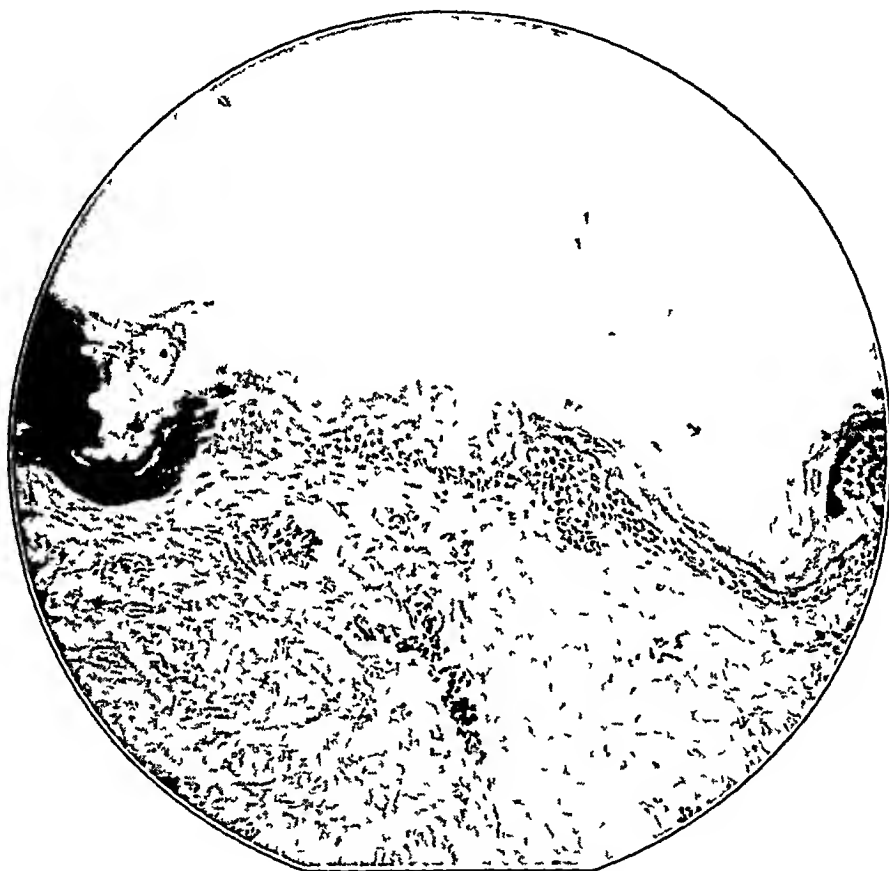


Fig 2 (case 1) —Photomicrograph of a section from the depigmented halo

The rete and basal cell layers were normal. There was acanthosis. Some of the interpapillary pegs were extremely long and narrow, and the free end was either spindle-shaped or bulbous. Some of these structures had a constricted neck and gave the impression that they were ready to be snared off. The basal layer contained a large amount of pigment. This was especially true of the swollen ends of the rete pegs. In the subpapillary zone were groups of cells with large, well stained vesicular nuclei and a good amount of protoplasm. There were no fibers between the individual cells, but the groups were separated by septums of connective tissue. Several large multinucleated cells were seen. Some of the cell groups were arranged perpendicularly in the form of long strands occupying the entire length of the papilla and almost reaching the apex, thus presenting a

picture of a typical intracutaneous pigmented nevus. A small number of lymphocytes were present in the corium. Pigment was not abundant in the nevus cells, and only a few islands were densely packed with pigment.

The silver stain revealed the absence of dendritic cells in the epidermis. Several cells which gave the appearance of chromatophores were seen in the cutis, but they were indistinct and could not be differentiated with certainty from the nevus cells.

From the pathologic changes it becomes evident that, at least in this case, the condition is probably not simple leukoderma or even vitiligo and that, except for the pigmentary disturbance, the deviations from the normal structure of the skin which we found in the excised patch are usually foreign to leukoderma or vitiligo. It is remarkable that these changes, which were fairly well defined in the microscopic section, were not so evident clinically. However, if we add to the pathologic observations the lack of response of the blood vessels of the white patch to external irritation as evidenced by the response to striking the area and to the application of a mustard plaster and the diminished sense of heat and cold, the picture becomes definite.

That the lack of response of the blood vessels to irritation may apply also to cutaneous reactions which are due to hematogenic causes is evident from the following case history.

CASE 2—While the patient in case 1 was still under observation, Dr Jacob Segal came with a youth about 19 to the office of one of us (Dr Feldman) for consultation about an eruption which was diagnosed as rubella. The eruption covered nearly the entire body, the macules were so numerous that they became confluent, and in places the skin was uniformly red. Among such red areas there was a white patch about 3 by 4 inches (7.5 by 10 cm) in diameter. Its location was in the lower part of the dorsal region. The outline was not round or oval but somewhat irregular. The borders were sharply demarcated, but they appeared to be scalloped. Occupying the center of this white patch was an elevated brown spot about 0.5 cm in diameter. This appeared to be an ordinary pigmented nevus. There were no macules or the slightest degree of redness within the limits of the white patch. The contrast between this and the congested skin was striking. There was a difference in temperature between the white patch and the affected surrounding skin. This difference could easily be determined by palpation. Without the presence of the central nevus one would not hesitate in diagnosing this condition as naevus anemicus. As it was, the findings in this case stimulated us to perform the simple experiments which were made on patient 1, and we were surprised with the results.

When the patient returned for reexamination several months later, the eruption was gone, but the achromic patch was still decidedly whiter than the normal skin. A number of enlarged capillaries were present at the border of the patch. This condition has been noted by a number of observers in naevus anemicus.

When the area which included the white patch was struck briskly with the palm, the normal skin became reddened but the color of the achromic patch remained the same. The same condition prevailed after vigorous friction. On pressure with the diascope the normal skin became blanched, but the achromic

patch was still whiter than the normal skin under the diascopé. There was diminished sensation for heat and cold. The tactile sense was as keen in the white patch as it was in the normal skin.

Injection of a 1:1,000 solution of epinephrine hydrochloride at the margin of the lesion caused blanching of the normal skin. As far as the achromic patch was concerned, it was difficult to say whether there was an increase in whiteness or not, but the portion of the achromic patch which was acted on by the epinephrine appeared to be somewhat lighter than the surrounding blanched skin.

An injection of 0.03 cc. of a 1:1,000 solution of histamine hydrochloride was made intradermally into the white patch and also into a normal area about 8 inches (20 cm.) distant as a control. A wheal with pseudopodia formed in each location. The one in the vitiliginous area was about 8 mm. in diameter, while the diameter of the one in the normal skin was about 6 mm. A deep red areola about 4 inches (10 cm.) in diameter formed about the wheal in the control. In the achromic patch the areola formed was much smaller and was very pale pink. In one location the areola included a portion of the normal skin outside the patch. This portion was deep red, not pink. One would judge that the proportion of depth of color between the areola of the achromic patch and that of the normal skin was 1:5. The redness within the white area disappeared within thirty-five minutes, while that of the control area was reduced by less than half in the same span of time. The wheal persisted longer in the achromic area than in the control area.

In order to verify these findings and for the purpose of comparison, we repeated the experiment on a patient with ordinary vitiligo. There was a difference in the depth of color between the areola in the area of vitiligo and that in the normal skin, but in spite of the fact that the surrounding skin was hyperpigmented, the difference was comparatively slight and could be easily accounted for by the difference in the original color.

Another and even stronger verification of our point of view that in the two reported instances of so-called Sutton's disease the patients had, in addition to the pigmentary disturbance, a disturbance in the circulatory mechanism, presumably due to improper innervation was furnished by the following case.

CASE 3—E. K., an 11 year old schoolgirl, came to the Morrisania clinic on Dec. 16, 1935, with an eruption of discrete red papules over the arms and trunk. The papules were arranged in lines, circles and semicircles, indicating a follicular distribution. There were two large patches, each about 4 by 5 inches (10 by 12.5 cm.) in diameter, on the left side of the trunk. Smaller patches were present, two on the right side and two on the back. The mother stated that the child had the condition since early babyhood but that she had not noticed it at birth. The papules appeared in the vitiliginous areas approximately in the same number as on the normally pigmented skin. The girl was a brunet, with a good amount of pigment in the skin, but the borders of the white patches were no more pigmented than the rest of the skin. If one is to stress the hyperpigmentation at the border as an essential diagnostic symptom of leukoderma or vitiligo, this patient's condition does not fall into that category. Is hyperpigmentation at the border of a depigmented patch overestimated as a symptom of these two conditions, or is the condition in this case something else, for instance the albinism partialis described by some authors?

When the eruption had cleared up, the reactions were tested in the same manner as those in the preceding cases, and no deviation from the normal function of the skin was found in the patch. Pressure with the diascopé did not obliterate the difference in color between the white patch and the normal skin. An injection of histamine hydrochloride at the border of the patch caused the formation of a

wheel and a bright red areola around it. The areola was situated partly on the normal skin and partly on the patch. The color was nearly uniform in the entire areola, and hardly a perceptible difference could be seen, in spite of the fact that the girl had a fairly dark skin.

From the study of the first two cases cited, one can readily see that the achromic area in so-called Sutton's disease is not necessarily a simple leukoderma but at times may show structural and functional changes which are usually not seen in leukoderma or vitiligo. In these two cases the functional changes, except for the pigmentary disturbance, were identical with those seen in naevus anemicus. Unfortunately, it was not possible to obtain permission for a biopsy in the second case, and for that reason it was not possible to ascertain the amount of depigmentation or apigmentation, if any. It was possible, however, to compare the clinical features with those in our first case or, for that matter, with any condition which might throw some light on the subject.

Soon the opportunity offered itself to us to compare the condition in this case with that in a case of frank naevus anemicus. This furnished us with what we thought to be valuable information.

CASE 4—R. R., a housewife, was admitted to the Morrisania City Hospital on Nov. 10, 1935, suffering from an acute gynecological condition. She received several injections of codeine sulphate and stated that she had taken acetylsalicylic acid before admission to the hospital. After she had stayed a few days in that institution, there developed a rubeola-like eruption on the front and back of the trunk, abdomen and lumbar region. On the back the eruption became confluent, to form a generalized scarlatiniform erythema, extending from the neck to the buttocks. In the sacro-iliac region there was a patch about $3\frac{1}{2}$ by $4\frac{1}{2}$ inches (87 by 112 cm.) in diameter. This patch was white and, as far as appearance was concerned, was unaffected by the eruption. The borders of the patch were sharply demarcated from the surrounding erythematous skin, and at the margin there was a comparatively large number of small white patches, ranging in size from that of a pinhead to that of a pea or larger.

The patient reported at the clinic on Dec. 2, 1935. At that time the eruption had disappeared, but the white patches were as clearly visible as they had been when it was present, although the contrast was not as marked. Pressure with the diascope made the patch invisible on account of the blanching of the normal skin. When the region of the white patches was struck with the palm, the normal skin became reddened, while the white area remained unaffected.

Injection of a 1:1,000 solution of epinephrine hydrochloride intradermally at the border of the white patch caused a blanching of the normal skin. The action of the epinephrine extended to a portion of the white patch, and this, together with the blanched normal skin, was considerably lighter than the rest of the white patch, which was not acted on by the epinephrine, indicating that, even in this location, a certain amount of color was due to circulating blood.

Tests of the reaction to heat and cold made in the same manner as those in the other cases showed a marked diminution of that sense in the white patch as compared with the normal skin. There was no difference in the sense of touch. Vigorous friction of the area with a pad soaked in turpentine caused reddening of the normal skin, while the white patch remained unaffected.

Injection of 0.03 cc of a 1:1,000 solution of histamine hydrochloride intradermally into the center of the white patch caused the formation of a wheal within a few seconds. This wheal gradually increased in size until when fully developed it measured about 1 cm in diameter. Surrounding this wheal a faint flush appeared immediately after the injection. The color was not uniform but gave the impression that certain capillaries were first to dilate. Soon, however, the color deepened to a light pink and formed a uniformly colored areola about the wheal. The same quantity of histamine was injected into the normal skin at the angle of the scapula. The wheal formed was somewhat smaller than the one in the white patch, but the surrounding areola which was formed immediately after the injection was much larger, about $2\frac{1}{2}$ inches (6.2 cm) in diameter, and deep red.

It was difficult to explain why the wheal formed after an intradermal injection of histamine hydrochloride in the white patch in naevus anemicus and in one of the cases of Sutton's disease described was larger than the one formed after an injection of the same quantity of histamine into the normal skin, whereas in the case of the areola the process was reversed, and the areola in the achromic patch was insignificant. Is it perhaps that the diffusion of the drug into the neighboring vessels and tissues was diminished in the affected region, the drug remaining confined mostly to the region injected and exerting a greater local influence on the vessels?

The only points of difference between naevus anemicus and the condition in the first two cases was that it was possible in the case of naevus anemicus completely to wipe out the difference in color between the affected area and the normal skin by simple pressure with the diascoposcope or by the injection of epinephrine hydrochloride at the border of the patch. It was not possible to obtain the same effect in the other two cases, and it was undoubtedly due to the diminution or absence of pigment.

CASE 5—A patient from the Mount Sinai clinic, 22 years of age, born in Puerto Rico, stated that she had observed the condition of her skin about two years before admission and that the lesions since that time had increased in size and in number. On examination there were noted about a dozen oval or rounded sharply defined areas, which were white and apparently devoid of pigment. In the center of each white area was an elevated light brown spot which resembled an ordinary pigmented nevus. The larger lesions were from 1 to $1\frac{1}{2}$ inches (2.5 to 3.7 cm) in diameter, the smallest not larger than a pea. They were scattered over the trunk and extremities. One lesion was situated on the vulva. A number of pigmented nevi without white halos occurred among the others. It was not possible to elicit from the history given by the patient whether the vitiliginous patch or the hyperpigmented central spot was the first to appear. To us it seemed that in one of the patches, at least, the white area was primary and the pigmented mole made its appearance in a preformed white patch. This was deduced from the fact that in the lesion referred to the central elevated spot was so minute when first observed that it was almost imperceptible and since then it had enlarged to the size of a large pinhead. A short time before her admission a new white patch without a central spot made its appearance.

The biopsy, made by Dr Samuel Peck, showed the presence of a typical nevus with typical nevus cells in one part of the section. There were practically no pigment cells in the central nevus. As a matter of fact, only one or two cells which contained melanin could be seen. This was demonstrated with the silver stain only. The rest of the section showed a rather thin epidermis with no other pathologic changes except that no pigment was to be seen in any of the basal cells or the overlying rete.

Application of a freshly prepared mustard paste over the region of one of the white patches caused a reddening of both the normal skin and the vitiliginous patch.

Injection of 0.03 cc of histamine hydrochloride into the white patch caused the formation of a wheal with a red areola. Injection of the same amount intradermally into the normal skin also caused a wheal and an areola which was deeper in color than the one in the white patch, but the difference in shade could be explained by the absence or presence of pigment.

Pressure with the diascope did not eliminate the difference in color between the white patch and the normal skin.

We availed ourselves of the offer of Dr I. Rosen to include this case from his service because it represented the reverse side of the medal—namely, no changes were present except the depigmentation. Even this is not entirely correct, as the section revealed a considerably thinner epidermis than is usual for the location from which the section was made.

In perusing the very meager literature on the subject one finds that the pathologic changes in the cases so far described are extremely variable. There seems to be a gradation from a nearly normal condition of the skin in the white patch to pathologic changes which are akin to real atrophy. Thus, depigmentation was incomplete in the case reported by von Poor, in which islands of pigment were found in the epithelium of the white patch. Most writers, however, have mentioned a normal but depigmented skin. There were other cases in which, excepting the achromia, there was the barest evidence of a pathologic condition, as in our case 5, in which the biopsy section revealed an epidermis which was thinner than was usual for the location from which the section was taken. Almkvist, on the other hand, did not mention any microscopic changes in the white patch in his case but stated that, in addition to the pigmented nevus in the center, the condition presented all the features of naevus anemicus. In our case, in addition to the clinical features of depigmentation and naevus anemicus, there were the pathologic changes of early atrophy, even including the degeneration of the elastic tissue which is so characteristic of atrophy. While this case has no parallel in the literature, it is backed up by the similarity of the clinical features to those of our second case and the case of Almkvist. We feel that had the pathologic changes in more of the cases reported been carefully studied the condition would not appear to be unique. On

the other hand, Lévy-Franckel, Guilhaume and Juster¹⁷ found edema and diminution, constriction and disappearance of capillaries in a patch of what appeared to be clinically ordinary vitiligo. Similarly, in speaking of vitiligo, Gans¹⁸ said that there are atrophic and inflammatory changes in the vitiliginous area along with nerve changes which are difficult to interpret.

Another characteristic of leukoderma acquisitum should serve to separate the condition in these cases from the general class of leukoderma and vitiligo. Chromatophores are supposed to be abundantly present at the margin of the lesion in leukoderma and in vitiligo, where they exert a phagocytic action on the melanin. In our cases, in those of Stokes and in others in which the pathologic changes were studied, chromatophores were conspicuous by their absence, hence there was no phagocytic action to explain the depigmentation.

So much for the pathologic picture. The clinical picture is as varied as the pathologic findings. Cases have been reported in which there were lesions consisting of a central mole with a surrounding white halo. In others these lesions were present in addition to achromic patches without central nevus, while in still others the patient had typical lesions of leukoderma acquisitum as well as achromic patches without centrally located pigmented spots and numerous pigmented nevi without white halos.

The central nevus varied from a small, insignificant and barely pigmented spot to a large, deeply pigmented, verrucous and hairy nevus. In one case lesions of molluscum fibrosum with white halos were present side by side with the typical lesion.

The regularity of the shape of the white patch, its almost constant round or oval configuration, with sharp borders, and its proportionate size to that of the central nevus indicate a rather more than casual occurrence of these lesions, and, to our way of thinking, there is no question that these lesions constitute a clinical entity. The existing uncertainty refers to their interpretation only. Those who consider the condition a primary and unusual form of vitiligo, the central spot being the reversal of the hyperpigmented border, will find solace in the fact that some lesions start as an achromic patch, the pigmented center developing later, while those who correctly consider the central spot a real nevus, the white portion being vitiligo which is caused by the presence of the nevus, will find apparent corroboration in the cases in which the lesion supposedly starts with a nevus and the white halo develops about it. On the other hand, if we take into account the findings of Leszczynsky, who stated that he saw the two lesions develop simultaneously, and

17 Lévy-Franckel, Guilhaume and Juster. Cutaneous Circulation in Alopecia Areata and Vitiligo, *Presse med* **33** 1050, 1925.

18 Gans, O. *Histologie der Hautkrankheiten*, Berlin, Julius Springer, 1925.

if we add to it the clinical and laboratory findings, which show a variation from a simple achromia to that of depigmentation plus the features of naevus anemicus, we cannot help being convinced that we are dealing with a nevus consisting of two component parts, one a true intra-cutaneous nevus which may or may not be pigmented and the other a nevus in the broader sense of cutaneous malformation. We assume that the central nevus may at times not be pigmented because of the reported findings of molluscum fibrosum, which may in reality be a true nevus, and because of the surprisingly small amount of pigment noted in the nevus cells in nearly all biopsy specimens.

Stokes' conception of the causation of the achromia appears to be the most plausible one, in spite of the fact that there were undoubted cases in which the vitiligo preceded the pigmented nevus at least clinically. We believe, however, that the two parts of the nevus originate simultaneously but that in some cases the pigmented nevus is so small that it is invisible on the surface, or the nevus may lack color and for the time be overlooked. It would be interesting to make serial sections of some of the achromic patches which occur in Sutton's disease and are clinically without a central nevus. This we hope to do when the opportunity offers itself. Our views coincide with those of Stokes only so far as we believe that the white lesion is caused by a physical or chemical disturbance in equilibrium of the tissues about the nevus. We cannot agree with him that the central nevus is the cause of that disturbance, but we believe that both the central nevus and the achromia are caused by a loss of tissue equilibrium which is congenital and is in accord with the theory of Connheim.

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PURPURA ANNULARIS TELANGIECTODES

REPORT OF A CASE

STUART C WAY, MD

SAN FRANCISCO

Majocchi¹ in 1896, after having observed three cases of a similar condition, described an unusual disease of the skin, characterized by the presence of minute telangiectatic puncta, which form various-sized annular lesions that disappear in the course of time, with or without atrophy

In 1915 MacKee² completely reviewed the literature and at the same time reported the thirty-ninth case

Among the more recent authors to describe this interesting disease are Copelli³ and Angelini,⁴ 1915, Semon,⁵ 1920, Balzer,⁶ 1926, Majocchi,⁷ 1928, Marchisio⁸ and Scholtz,⁹ 1929, Gottron,¹⁰ Cavallucci,¹¹ Curle and Smith¹² and Way,¹³ 1930, Ciarrocchi¹⁴ and Selissky,¹⁵ 1931, Ferrabouc, Massia and Friess,¹⁶ 1932; Nordin¹⁷ and Levin and Tolmach,¹⁸ 1933

From the Department of Dermatology, Mary's Help Hospital

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REPORT OF CASE

Mrs W B, aged 32, a housewife and resident of Santa Rosa, Calif, was born in California of Danish-American parents. She had always lived on a farm and been accustomed to heavy work. Her father died of heart disease at the age of 75. Her mother died of cerebral hemorrhage. An infection due to *Trichina* caused the death of one sister. There was a definite history of tuberculosis on the father's side of the family, several members having been affected.

The patient had the usual diseases of childhood, including varicella, whooping cough and scarlet fever. Menstruation began at the age of 11. A complete hysterectomy was performed on the patient at the age of 26. There were two children, a boy aged 10 and a girl aged 11.

In the fall of 1932 the patient had a severe infection of the antrum, which subsided as soon as drainage was established. Her physician stated that a culture of the material from the antrum was not made. At the time of this infection a dermatitis developed about the ankles, which resembled the present cutaneous involvement. Three or four months elapsed before it disappeared.

During the fall of 1933 there was a recurrence of the sinus infection and of the dermatitis about the ankles. Apparent recovery from both took place as before, in the same length of time.

On Dec 21, 1934, the patient called at the office, complaining of a dermatitis limited to the lower extremities, which had itched intensely since its onset, six weeks before. The cutaneous manifestations, as in previous years, followed a severe infection of the sinus.

Physical Examination—On examination the patient appeared to be of normal intelligence, free from all neurotic tendencies. Her height was 5 feet, 2 inches and her weight 200 pounds (90.6 Kg). The infection involving the antrum had temporarily cleared up. A few varicella scars were present about the face, but scars suggestive of syphilis, tuberculosis, etc., were lacking. Minute superficial varices, commonly seen about the legs, were also absent, and except for the eruption and considerable dermographia nothing unusual could be detected.

Description of the Eruption—The eruption was located on the anterior and lateral surfaces of the legs, between the ankles and the knees and also about the ankles, where it was most profuse. The mucous membranes and other parts of the body were not involved.

The earliest lesions, of macular type, varied in size from that of a pinpoint to that of a pinhead, were bright red and occurred independently of hair follicles.

Diascopic pressure caused a paling of the lesions but no alteration in the color of the hemorrhagic dots. The lesions enlarged by peripheral extension to a diameter of from 3 to 4 cm and cleared centrally but left a brownish pigment, while the reddened borders contained innumerable telangiectatic puncta. The occasional joining of annular lesions produced varied configurations. Furfuraceous scaling was also present. The sites of the older lesions were indicated by brown pigmentation of various shades, depending on the age of the lesion, but atrophy, noted by some observers, could not be detected. Various-sized pale red elevated papules, clinically characteristic of urticaria, were present on the anteroposterior and lateral surfaces of the knees. These lesions lacked the hemorrhagic puncta, telangiectasia and pigment common to purpura annularis telangiectodes.

Laboratory Examination—The Kolmer, Kahn and Pirquet tests gave negative results. The blood count showed leukocytes 18,760, erythrocytes 4,630,000 and

platelets 288,000 The coagulation time was three minutes and forty-two seconds The hemoglobin content was 80 per cent (Sahl), and the color index, 0.97 The differential count was as follows polymorphonuclears 53 per cent, lymphocytes 27 per cent, monocytes 16 per cent, eosinophils 3 per cent, basophils 1 per cent, segmented polymorphonuclears 44 per cent and banded polymorphonuclears 9 per cent

The urinalysis showed specific gravity 1.018, no albumin or sugar and an acid reaction A centrifugated specimen showed many oxalate crystals and numerous epithelial cells, about 6 per high power field There were 4 pus cells per high power field

Biopsy—A section of skin representing the hemorrhagic pigmentary stage of the disease was removed from the outer surface of the left ankle The tissue was fixed in alcohol, embedded in paraffin, cut in serial sections and stained as follows with hematoxylin and eosin, hematoxylin and orange "G," polychrome methylene blue, Gram's iodine, and orcein, by Weigert's, Giemsa's, Pappenheim's and Ziehl-



Fig 1—Area from the outer aspect of the left ankle One of these isolated lesions was removed for microscopic study

Neelsen's methods and according to Perles' test for prussian blue reaction for hemosiderin

Microscopic Study—Under low power one noticed an increase in the number of small capillaries, they were dilated, and cellular infiltration surrounded them and the coil glands This vascular dilatation occurred throughout the dermis and the subcutaneous tissue

Epidermis The stratum corneum was moderately thickened, and perifollicular parakeratosis could be noted in practically all of the sections This parakeratosis caused the occlusion of many of the sweat-gland ducts, and their consequent dilatation in some instances involved the body of the gland itself Several sections showed enormously dilated ducts, occurring within the epidermis, which were completely filled with various products of excretion together with a few leukocytes Inter-cellular edema and epidermal necrosis explained in part the interference with the normal evolution of the epidermal cells and accounted for the thickening of the

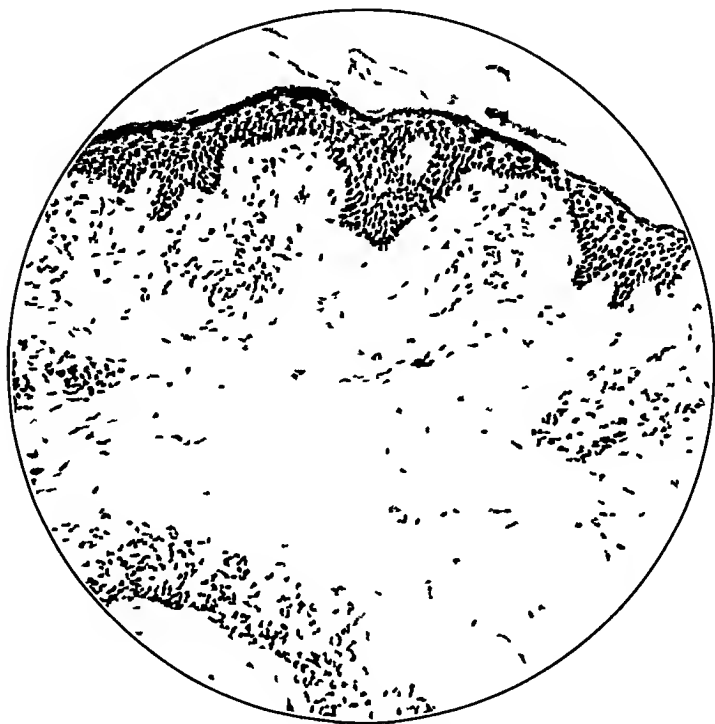


Fig 2—The vessels throughout are dilated and surrounded by infiltrating cells
Hematoxylin-eosin stain, $\times 120$

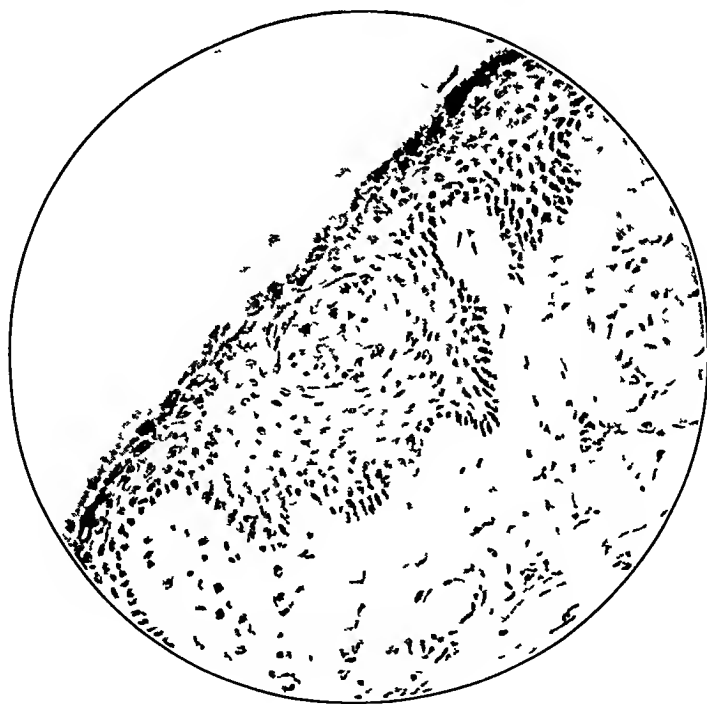


Fig 3—Dilated sudoriparous duct within the epidermis, containing leukocytes
and other products of excretion Weigert's hematoxylin stain, $\times 300$

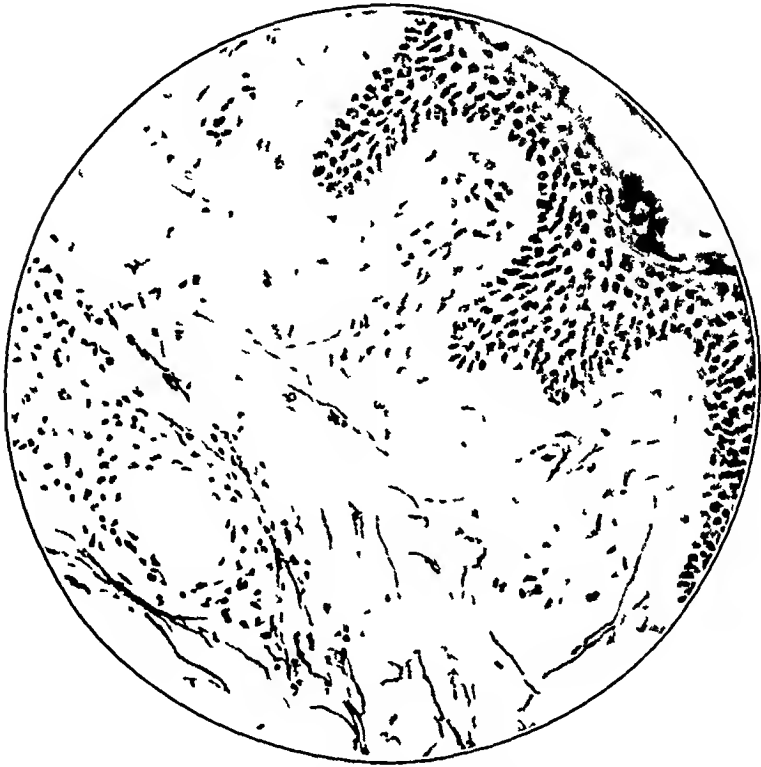


Fig 4—Papillary edema, vascular dilatation and an enormously distended sudoriparous duct Weigert's hemtoxylin stain, $\times 200$

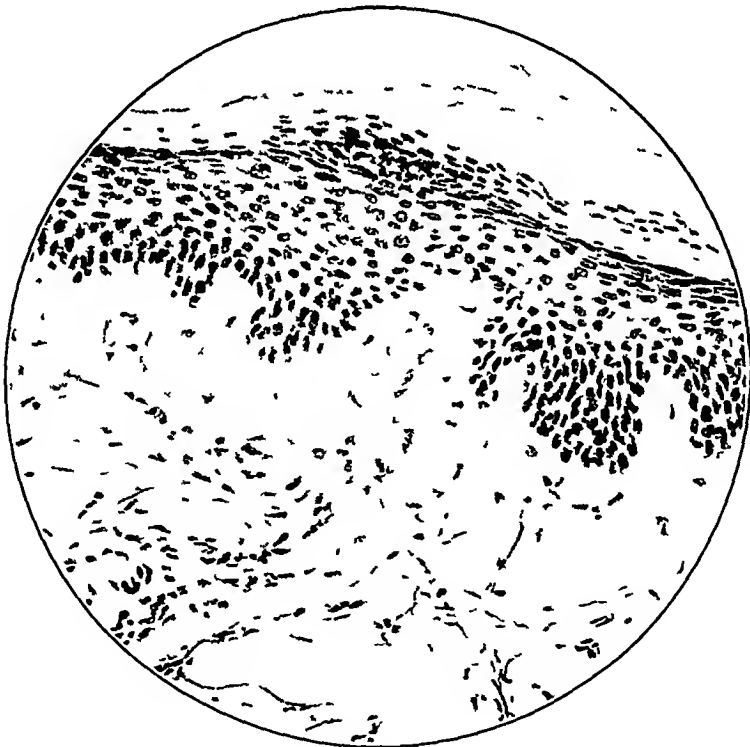


Fig 5—Parakeratosis and an epidermal micro-abscess Weigert's hematoxylin stain, $\times 300$

corneum and the exfoliation which Highman¹⁹ has mentioned. Nonhematogenous pigment occurred extracellularly and intracellularly near and within the basal layer.

Dermis The upper layers of the dermis, especially the papillary layer, were edematous. There was a distinct increase in the number of the smaller capillaries, and although they were widely dilated, hemorrhage as a result of the rupture of a capillary or diapedesis could be neither observed nor demonstrated by Perles' test.

Throughout the subpapillary layer many of the vessels presented alterations in their walls. In some the endothelium had proliferated and become swollen and caused almost a complete occlusion of the lumen. Tiny aneurysmal sacculations in longitudinal sections were occasionally seen in the walls of the vessels, when the wall was thin and ballooned out. Near by were extravasations of serum. Although this vascular dilatation persisted throughout the deeper part of the dermis and also within the subcutaneous tissue, few of the vessels were filled with blood.

The infiltrating cells, consisting of lymphocytes, endothelial cells and eosinophils, were noticeably dense about the subpapillary vessels and the sudoriparous glands and ducts.

The elastic fibers were apparently normal, except in the infiltrated areas, where they were either swollen or completely absent.

The degree of degenerative change that the sweat glands showed seemed to depend on the density of the infiltrating cells, but in no instance had the glands completely disappeared. A few of their ducts were widely dilated.

The hair follicles and sebaceous glands were little affected. Sections stained by Ziehl-Neelsen's method gave negative results for acid-fast bacilli when examined by Hoffmann's²⁰ dark-field method.

COMMENT

The following factors in this case coincided with Majocchi's original description of the condition: (1) the appearance of the eruption, except for the follicular occurrence, (2) the slow, progressive development by peripheral extension and the formation of annular lesions, (3) the symmetrical distribution of the lesions and (4) the location of the eruption, that is, the fact that it was present only on the extremities.

In the following respects the case under consideration differed from that observed by Majocchi: (1) in the intense pruritis (all lesions), (2) in the tendency to recur annually, (3) in the coexistence of the infection and papular urticaria, (4) in the absence of terminal atrophy, and (5) in the fact that the condition followed a definite sinus infection.

Although several authors, including Majocchi,¹ Ossola²¹ and Verrotti,²² have commented on the pruritus which preceded the eruption,

¹⁹ Highman, W. J. *Dermatology*, New York, The Macmillan Company, 1921, p. 86.

²⁰ Hoffmann. *Die Bedeutung der Leuchtbildmethode zur Darstellung von Mikroorganismen*, *Dermat. Ztschr.* **33** 6, 1921.

²¹ Ossola. *Gior. ital. d. mal. ven.* **46** 250, 1911.

²² Verrotti, G. *Gior. internaz. d. sc. med.* **33** 167, 1911.

I do not believe that in these cases the condition was complicated by coexisting urticaria. Apparently in this case the two diseases occurred independently of each other, for in July 1935 typical papular urticaria again appeared on the patient's lower extremities, but there was no evidence of purpura and the eruption disappeared within a few days, without pigment formation.

The pathologic picture in this case was in close agreement with that in the cases already reported, but, as in MacKee's²³ description, the amount of hemorrhage noted microscopically was almost negligible, although clinically considerable appeared to exist. As has been stated, this clinical picture may be due to the fact that thrombosed or angiectatic superficial capillary loops are dark red, fail to pale on pressure and may simulate hemorrhagic puncta.

A more definite relation to infection seems to be established in the instance under consideration than in the cases previously reported. The infection of the antrum from which the patient suffered at the time of examination seemed to be the explanation for the leukocyte count of 18,760. Recurrence and remission, such as those described in this paper, have been called a part of the clinical picture of purpura annularis telangiectodes.

SUMMARY

A case of purpura annularis telangiectodes occurring simultaneously with urticaria is reported.

Acid-fast bacilli and Russell fuchsin bodies could not be found.

The microscopic changes suggested that the disease was due to a toxin.

The theory of toxic origin seems to be substantiated by the fact that the cutaneous manifestations for three successive years were preceded by a severe sinus infection.

²³ MacKee, G. M. *J. Cutan. Dis.* **33**: 187, 1915.

ETIOLOGY, PATHOLOGY AND TREATMENT OF LEUKOPLAKIA BUCCALIS

WITH A REPORT OF THREE HUNDRED SIXTEEN CASES

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Leukoplakia buccalis, leukokeratosis or smoker's patch is one of the most common lesions that one encounters in an examination of the oral cavity. A voluminous literature has been written on the subject over many years, and yet several facts about the condition need to be elucidated. It is interesting to note how the authorities differ regarding the relation of syphilitic infection to the development of leukoplakia, and a free discussion by various observers leads invariably to a considerable difference of opinion as to whether syphilis is the most important causal factor.

For the past several years I have classified the cases of this condition in relation to the etiology and studied the histologic changes in the various stages of development of the lesion.

This study of leukoplakia was carried on primarily at the clinic in oral medicine at Tufts Dental School and was extended to include a group of cases observed in the department of dermatology and syphilology of the Boston City Hospital and in private practice. The cases have been studied with particular reference to the incidence of syphilitic infection and to the use of tobacco in its various forms.

GRADES OF LEUKOPLAKIA

In order to indicate properly the types of leukoplakia, I have graded its stages according to the clinical and histologic picture.

Grade 1—This type is characterized by the initial reaction of the mucous membrane to irritation, indicated by a red, granular, sharply defined, slightly sensitive area, which remains in this stage a short time and later becomes slightly whitish gray. The microscopic picture of the lesion shows a purely inflammatory reaction of the corium, without definite epithelial proliferation.

Grade 2—In this stage a definite lesion occurs, it is characterized by bluish-white patches or plaques, without palpable induration but sharply outlined from the normal mucosa. The lesion is quadrangular

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or irregularly polygonal, and the plaques appear to be pasted on the mucous membrane. Microscopically there is a definite hyperkeratotic and acanthotic change, with a slightly cellular reaction in the corium.

Grade 3—This grade of leukoplakia is definite and is easily recognized at a glance, even by a layman. It presents a milk-white, pearly or silvery indurated plaque, which may be localized or may cover a large area. The lesion may tend to wrinkle, especially if it involves the buccal mucosa of the cheeks. Microscopically the classic picture of



Fig 1—Photomicrograph of a lesion from a smoker's palate (fig 2), showing grade 3 leukoplakia

marked hyperkeratosis with acanthosis and cellular reaction of the corium is seen.

Grade 4—This stage, clinically, is observed as a still more pronounced keratotic lesion, indurated and leathery and beginning to show evidence of malignancy, which is recognized by early erosion, by fissuring of the plaque or by the tendency to warty proliferation of the surface. This grade should be treated as an incipient malignant neoplasm.

CLASSIFICATION OF LEUKOPLAKIA ON THE BASIS OF ETIOLOGY

To simplify the classification of the types of leukoplakia from an etiologic standpoint, I have grouped the cases as follows those in which the condition was due to (1) faulty occlusion, (2) chronic irritation, (3) use of tobacco and (4) syphilis

Group 1 Faulty Occlusion—This group was the largest in my collection of cases. On examination of the oral cavity, localized areas of leukoplakia due to faulty occlusion, caused by either natural teeth or artificial partial or full dentures, may be observed in an appreciably large number of persons, especially in those beyond middle life, in whom the irritation has continued over many years. However, it is interesting that in this large group the additional factor of use of tobacco plays an important rôle. Since its use is so general and since it acts as an associated irritant in the cases of leukoplakia due to faulty occlusion, the two factors frequently have to be considered together. Often there is malocclusion which has affected the patient from childhood and has never been properly corrected, the contact irritation of the delicate mucous membrane is an important factor in the production of leukoplakia. This type is more common in the buccal mucosa of both cheeks and is usually a bilateral process, as the occlusal factor is symmetrical. An important type of occlusal disturbance is related to the previous loss of one or more teeth and the use of the gingival margin as a biting surface, so that considerable irritation is brought to bear on the edentulous gingival margin. This condition is particularly common in the region of the third molar when the tooth has failed to erupt or has been removed. It is interesting that in younger persons it is not uncommon to find a tendency for the teeth in apposition to the edentulous gingival crest to protrude from their sockets, to compensate for the lack of dental articulation. A careful search of the oral cavities of persons with dental occlusal defects, especially of those beyond middle life, reveals an extraordinarily high percentage of localized leukoplakic lesions. Most of them, however, are relatively mild and require no treatment, and the introduction of proper bridgework to fill in the dental gaps or the grinding of the occlusal edges of sharp teeth is usually effective in controlling the condition. There is a type of malignant process which begins in the mucous membrane of the gingiva and extends to the jaw by continuity. A focal leukoplakic lesion initiates the epithelial neoplasm, but as carcinoma of the jaw does not arise primarily in bone it is reasonable to assume that the so-called primary carcinoma of the maxilla arises in a leukoplakic lesion of the gingival or adjacent mucosa. In a series of male patients taken at random, who were definitely nonsyphilitic, faulty occlusion was the most common single cause. In women the condition, in the few cases that I have noted, was due to faulty occlusion or to chronic irritation in the oral cavity.

Leukoplakia of the tongue in women is invariably associated with atrophic glossitis due to primary or secondary anemia. In general one may say that the frequency of the condition increases greatly in persons over 40 years of age, especially in those who use tobacco to excess.

Group 2 Chronic Irritation—In this group are included the cases of focal irritations of the mouth other than those in which the condition is due to the use of tobacco, which I have grouped by themselves. Among the causes of local irritation, other than faulty occlusion, are carious teeth, oral electric currents, sharp edges of crowns and bridges, lingual bars and other dental appliances, habitual biting of the cheeks and lips and hot and spicy foods, the latter significant especially in cases of leukoplakia involving the tongue. I have also included in this group the case of the man who chews tobacco and who usually carries the cud in contact with the buccal mucosa of the cheek. A factor that is important in all cases of leukoplakia, but is especially so in this group, is chronic periodontal infection, with associated lack of dental hygiene. I am convinced that the edentulous mouth, with artificial dentures that fit properly or without them, tends to remain free from leukoplakia. The betel nut quid is a common cause of leukoplakia and of malignant growths of the oral cavity. It is made up of tobacco, betel nut and black catechu. The chewing of this quid liberates various pigments, gallic and tannic acid, oils and bitter substances. The incidence of leukoplakia and of malignant conditions from this type of irritation is about equally divided between the sexes.

Recently there has been considerable literature on the presence of electrolytic currents in the oral cavity¹. I do not believe that this factor is important in causing focal irritation with resulting secondary leukoplakia.

An improperly vulcanized plate may be a source of chemical irritation, with the secondary development of leukoplakia.

Group 3 Tobacco—The use of tobacco is generally recognized as the most important factor in the production of leukoplakia and the most frequent cause². To be sure, the irritation due to tobacco is superimposed on other types of irritation, but even by itself it is generally considered to be the outstanding irritative agent in the production of the condition. It is generally accepted that the products of combustion and heat are the underlying sources of irritation to the mucous membrane. Various observers have indicated that the last few centimeters of a cigaret contains a concentration of irritating substances which are

1 Lam, E. S. Chemical and Electrolytic Lesions of the Mouth Caused by Artificial Dentures, *Arch Dermat & Syph* 25:21 (Jan) 1932.

2 Hollander, L., Permar, H. H., and Shonfield, L. Leukoplakia of the Oral Mucosa, *J Am Dent A* 20 41, 1933.

highly injurious to the mucous membrane. From my studies I am convinced that the use of the pipe is by far the most irritating form of smoking. It is difficult to say which is the greater offender in causing leukoplakia, the cigaret or the cigar. As heat is undoubtedly an important factor, I assume that the cigar, especially if it is smoked to the extreme end, generates more heat than the cigaret and therefore, other conditions being equal, would produce more irritation. The tar and nicotine content and the many other injurious irritants in tobacco combine to produce local irritation.

The method of smoking seems to play an important rôle in the localization of leukoplakia. One-sided smokers tend to produce a unilateral involvement, especially of the tongue. Many smokers tend to inhale



Fig 2—A smoker's palate, with grade 3 leukoplakia

the smoke into the oral cavity in the form of a funnel, and when it is brought into frequent contact with the mucous membrane in the region of the palate, localized plaques of leukoplakia are produced. Probably the most common location for leukoplakia, even more common than the lips, is the buccal mucosa at the angles of the mouth. This fact suggests that the exhalation of smoke through the corners of the mouth is an important source of irritation.³ The use of the smooth amber mouth piece, in contrast with the old clay pipe, is unquestionably significant in lessening heat as a source of irritation to the lip and tongue. The person who tends to keep the tongue in contact with the end of the cigaret or cigar often has involvement of the tip and anterior margin

³ Landouzy, L. Leucoplasies jugales et commissurales, *Presse med* 16 409, 1908

of the tongue It is rare to find leukoplakia of the dorsum of the tongue in a nonsmoker, even the patient with a preexisting syphilitic glossitis does not have leukokeratosis of the atrophic mucous membrane unless he is addicted to the use of tobacco Among the products found in tar and cigaret smoke are nicotine, phenolic bodies, pyridine bases and ammonia The last $\frac{1}{2}$ inch (1.3 cm) of a cigaret shows a definite accumulation of irritating substances, particularly of tar and other products of incomplete combustion Rapid smoking produces a rapid rise in temperature within the oral cavity, and smoking to the extreme end definitely increases local heat There is no question that heat and the irritation from the products of combustion are the most important causes of the reaction of the tissues that culminates in leukoplakia



Fig 3—A lesion occurring on the tongue of a right-sided, nonsyphilitic smoker, grade 3 leukoplakia

Group 4 Syphilis—There is a wide divergence of opinion even today as to the relation of syphilis to leukoplakia The confusion is undoubtedly due in part to the observations of the older writers, who invariably connected most cases of leukoplakia with syphilis

After studying 316 cases of leukoplakia, I am convinced that in a high percentage of cases extensive involvement of the tongue is definitely related to syphilis but that there is no evidence to indicate a relation between the greater number of instances of leukoplakia observed elsewhere in the oral cavity and syphilitic infection The predisposing factor in leukoplakia linguae is atrophic glossitis of syphilitic origin, occurring in untreated or inadequately treated patients with syphilis of long standing This type of glossitis, with the secondary sheen of hyperkeratotic leukoplakia, presents a picture almost pathognomonic

of syphilis⁴ This variety of leukoplakia was recognized by the older observers and gave rise to the popular idea that leukoplakia was always of syphilitic origin A characteristic picture of leukoplakia linguae is smooth red atrophic areas interspersed with more or less generalized leukoplakic lesions Frequently there is a modification of the type of glossitis, and the tongue is involved in a sclerotic process with secondary lobulation, due to the contraction of interstitial connective tissue The same surface leukokeratotic process is usually associated with this type of glossitis In contrast to the picture presented by syphilitic glossitis is that of the reaction of the normal tongue in heavy smokers, in whom the hypertrophy and leukoplakia are confined to the papillae, producing a thick, roughened, whitish surface

I recently had an opportunity to study at autopsy a case of carcinoma of the tongue, secondary to syphilitic glossitis (atrophic type) with secondary leukoplakia Considerable endarteritis with narrowing



Fig 4—A smoker's palate, in the early stage of involvement, showing the umbilicated orifices of mucous glands

of the lumens of the small vessels was noted These observations suggested a reasonable theory for the production of the so-called bald tongue or syphilitic atrophic glossitis, which may be due to the following mechanism

The tongue is an organ that may receive a heavy dose of spirochetes in the secondary stage of syphilis, with resulting endarteritis Later, because of the interstitial sclerosing process in the patient that is inadequately treated or untreated, there results a secondary atrophy of the papillae, which are terminal epithelial tissue complexes of special function The atrophy is undoubtedly due to the decrease in the blood supply resulting from the preexisting endarteritis As a result of atrophy of the papillae on the dorsum of the tongue, this organ is left "naked" and exposed to irritation from the products of combustion in smokers,

⁴ Gastou and Tremolliere Leukoplasie linguale syphilitique, Bull et mem Soc anat de Paris 88 49, 1903

and other forms of irritation give rise to the protective production of epithelial plaques of leukoplakia

The leukoplakic tissue in turn tends toward malignant growth, this explaining the high incidence of carcinoma of the tongue in patients with syphilis ⁵

Constitutional factors have been suggested as important in predisposing a person to leukoplakia or in actually causing it

A lack of vitamin A may result in atrophy of the lingual papillae and predispose the patient to lingual leukoplakia. A hereditary predisposition to degeneration or atrophy of tissue, allied to so-called cancer susceptibility, may be a factor

Syphilis, as has been indicated in this study, is only one factor in the development of the lingual condition, and a possible mechanism explaining the production of the condition has been described



Fig 5—Atrophic syphilitic glossitis with leukoplakia of the tongue and verrucous squamous cell carcinoma of the external commissure. With electrocoagulation a five year cure was effected

Atrophic glossitis occurs in prolonged secondary and also in pernicious anemia, probably as a result of impoverishment of the blood supply of the tongue. In such cases leukoplakia may occur independently of irritation caused by tobacco, and is a result of the use of hot or spicy food. The rare leukoplakic lesion of the tongue in women is usually secondary to the bald tongue of severe anemia

Incidence—Leukoplakia is overwhelmingly prevalent in men, only a small percentage of cases have been noted in women ⁶. This overwhelming disparity between the sexes may change in the course of time, since women have taken up the use of tobacco, and after a number of years one might expect to see the disease more common among them

⁵ Sturgis, Somers H, and Lund, Charles C. Leukoplakia Buccalis and Keratosis Labialis, New England J Med 210 996, 1934

⁶ Hazen, H H, and Eichenlaub, F J. Leukoplakia Buccalis, J A M A 79 1487 (Oct 28) 1922

DIFFERENTIAL DIAGNOSIS

The diagnosis of leukoplakia should not be difficult, as the lesion in most cases is definite and characteristic, especially in grade 3 and grade 4 of the condition. However, there are a few conditions which simulate leukoplakia.⁷

1 Syphilitic lesions. There is a type of chronic mucous patch which presents a silvery sheen and which may resemble leukoplakia but, of



Fig 6—Photomicrograph of a lesion of oral lichen planus, showing decided acanthosis, slight hyperkeratosis and a sharply outlined zone of cellular infiltration, $\times 100$

course, is accompanied by other signs of syphilis, proper antisyphilitic treatment causes the disappearance of this lesion.

2 Lichen planus. Clinically it is difficult in certain cases of oral lichen planus, in the absence of lesions elsewhere on the body, to differentiate the condition from leukoplakia. However, in lichen planus the

7 Fox, H. Leukoplakia Buccalis, J A M A 85 1523 (Nov 14) 1925

characteristic picture is usually that of slightly raised fine papules, with dendritic whitish lesions, which tend to be symmetrical and are usually found in the buccal mucosa of both cheeks. Extensive involvement, however, may affect the tongue, particularly the lateral margins, the floor of the mouth and the lips. The two sexes are affected more or less equally with this disease. In the vast majority of cases there is an associated characteristic papular violaceous rash with angulated shiny papules involving the extremities. The microscopic picture may also be confused with that of leukoplakia, but in general in cases of lichen planus the hyperkeratotic reaction is less pronounced or even absent, and the cellular reaction of the corium is far more intense and sharply demarcated, tending to obliterate the rete cones.

3 Oral lupus erythematosus. This disease occasionally invades the lips and oral cavity by continuity from facial cutaneous lesions. The lesions usually are painful, with superficial ulceration surrounded by a zone of whitish tissue, resembling leukoplakia. They are irregularly distributed, a biopsy shows the loss of epithelial surface from the focus of ulceration and considerable cellular infiltration of the corium. Lesions which may be present elsewhere on the body help to differentiate the condition.

4 Exudative processes in the mouth. These can be differentiated from leukoplakia by the fact that the exudate can be readily removed by mechanical means, leaving a raw inflammatory surface.

COURSE OF DISEASE

The course of the disease depends entirely on the cause and on preventive and local treatment. In some cases the removal of the irritating factor, as in the occlusal and irritative group, favors the disappearance of the lesion.⁸ In cases of pronounced involvement due to irritation from the use of tobacco the lesion tends to persist indefinitely but not to increase. The conditions comprising grade 1 and grade 2 have a tendency to disappear after removal of the causal factor. The symptoms of the lingual syphilitic type in which there is a preexisting atrophic glossitis, continue, and the condition has to be watched closely for evidence of a malignant lesion.

RELATION TO MALIGNANT GROWTHS

There is no question that leukoplakia is a forerunner of a malignant process.⁹ It corresponds in pathologic changes to the keratotic lesion of

8 Spencer, W. G., and Cade, S. *Diseases of the Tongue*, Philadelphia, P. Blakiston's Son & Co, 1931, p. 173.

9 Bloodgood, J. C. Summary of Etiologic Factors and Resultant Lesions in Cancer of Oral Cavity, Especially in Relation to Prevention of Malignant Disease and Preservation of the Teeth, *J. Am. Dent. A.* 19:1738, 1932.

the skin. The subsequent malignant growth is always of the squamous cell type, but the malignancy tends to be of low grade, making the prognosis more favorable. The ulcerative, indurated type of leukoplakia develops into a growth with the highest degree of malignancy¹⁰. It is difficult to demonstrate the preexisting leukoplakic lesion in a case of malignant growth, especially if the malignant growth has developed to a point where the original hyperkeratotic process cannot be demonstrated and if the patient has failed to observe the preexisting process. A malignant involvement of the tongue is preceded by syphilitic leukoplakia in a high percentage of cases. Leukoplakia of the margin of the gums due to faulty occlusion gives rise to so-called malignant disease of the jaw. Statistics on the percentage of malignant processes arising from preexisting leukoplakia are necessarily inaccurate, as in most cases the local leukoplakic lesion has been obliterated by the neoplasm.

TREATMENT

Except for the preventive form of treatment, the removal of the irritating factor in the mouth and abstinence from the use of tobacco, the treatment of leukoplakia is unsatisfactory¹¹. When the use of tobacco is an etiologic factor and the patient continues to use it, the removal of the leukoplakic lesion is usually followed by a recurrence. I have used various methods of treatment in leukoplakia and have essentially given up the use of radium and of roentgen therapy, confining myself to the use of electrodesiccation and electrocoagulation by monopolar and bipolar high frequency current. I have not used the actual cautery, but I believe it is equally effective. I feel that the use of radium in the treatment of leukoplakia of the tongue associated with atrophic syphilitic glossitis is provocative of a malignant growth when the treatment is given in small doses over a long time. A malignant process has developed in 2 of my cases after this type of treatment, with the radium plaque administered in 5 mg and 10 mg doses for from twenty minutes to one-half hour. Treatment over months ultimately resulted in the development of processes of verrucous carcinoma. It is advisable for the physician with a patient suffering from this condition to insist that he stop all smoking, to keep him under close supervision and to use monopolar or bipolar electrocoagulation to destroy any lesion which tends toward malignant change. Multiple malignant growths of the tongue develop in this type of case, and great care

10 Bofeldt, S. A. Pathologische anatomische und klinische Studien über die Leukoplakien der Lippen und deren Verhältnis zum Carzinom, *Arch. d. path. Inst. d. Univ. Helsingfors* 22: 325, 1927.

11 Prinz, H. Leukoplakia Oris. A Clinical Study, *Dental Cosmos* 70: 663, 1928.

should be exercised in the examination of the patient. It is desirable that the patient report every few months. I have seen in a few cases a malignant process develop to an inoperable stage owing to the neglect of the patient to keep in touch with the physician or clinic. The vast majority of leukoplakic conditions require no treatment. The use of locally applied irritating or caustic remedies is contraindicated, as there is a possibility of stimulating malignant change in the lesion. The surgical removal of the malignant lesion is indicated in some cases, but I have found that in cases of leukoplakia involving the tongue this procedure is often carried to a more radical degree than necessary and the electrical current is preferable.

CONCLUSIONS

A study of 316 cases of leukoplakia is reported, with reference to the etiology and clinical gradation of the condition.

Only in cases in which the condition involves the tongue can it definitely be determined that syphilis plays a rôle in the etiology of leukoplakia.

Leukoplakia can be considered a definite forerunner of malignant growths.

Tobacco is by far the most important direct or indirect factor in the production of leukoplakia.

The mechanism involved in the production of syphilitic glossitis with leukoplakia is described.

KERATODERMA AND MELANODERMA ACCOMPANYING THERAPY WITH A GOLD COMPOUND

REPORT OF A CASE

S IRGANG, M D

NEW YORK

Cases have been reported in which cutaneous hyperpigmentation appeared on the site of gold dermatitis subsequent to its resolution. There are no reports concerning the development of primary melanoderma, that is, of the spontaneous appearance of hyperpigmentation, without relation to a preexisting eruption. Likewise a search of the literature failed to reveal any reference to a concomitant production of excessive melanotic pigment in the active lesions of gold dermatitis.

It is well known that the cutaneous reactions accompanying aurotherapy are multiform. They may appear as exfoliative dermatitis or urticaria or may simulate erythema multiforme, scarlatina, lichen planus, pemphigus or pityriasis rosea. There are few references in the literature to the occurrence of keratoderma following this type of therapy, a condition which is admittedly rare.

Pardo-Castello,¹ in discussing a paper by Driver and Weller, briefly reported a case of symmetrical palmar hyperkeratosis which appeared after six injections of 50 mg each of sodium aurothiosulfate (Mollgaard). This reaction occurred in a woman, 35 years of age, who had chronic lupus erythematosus of the face.

Rabut² reported a second case of keratoderma following therapy with a gold compound. The patient was a woman, aged 47, in whom exfoliative dermatitis developed after she had received nine weekly injections of allochrysin (sodium thio-auroglycerinsulfonate) of 100 mg each for "tuberculous rheumatism." After resolution the dermatitis was replaced by melanoderma on the site of the previous exfoliative dermatitis and by a keratotic nodular eruption of the scalp, back, chest, lower extremities and mouth.

The following report concerns the development of keratoderma and melanoderma during a series of injections of gold sodium thiosulfate.

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1 Pardo-Castello, V, in discussion on Driver, J R, and Weller, J N. Untoward Results from the Use of Gold Compounds, Arch Dermat & Syph 23: 87 (Jan) 1931.

2 Rabut, R. Le keratoderma cause par l'emploi de l'or, Bull Soc franç de dermat et syph 38: 463 (March) 1931.

REPORT OF CASE

A Negress aged 27 presented chronic superficial lupus erythematosus of one year's duration. It was limited to the nose and consisted of two plaques, the larger covering practically the entire lower third of this area and the smaller situated slightly above and to the left of the larger. There was no involvement of the oral mucosa. The patient had not been treated prior to her admission to the clinic. From July 2, 1935, to Sept 17, 1935, she received twelve weekly intravenous injections of gold sodium thiosulfate. The dose was for the initial injection, 10 mg, for the second, 20 mg and for each of the succeeding ten treatments, 25 mg. At no time did she complain of systemic symptoms that were ascribable



Fig 1—Secondary melanoderma of the nose (on site of previous lupus erythematosus) and primary melanoderma of the left side of the face. The hyperpigmentation of the vermillion border of the lips is not visible. The palmar aspects of both hands are decidedly thickened as the result of intense hyperkeratosis (Photograph reproduced through the courtesy of Dr Howard Fox)

to an idiosyncrasy to the drug. The eruption was resolved completely after the seventh injection, that is, after the patient had received 155 mg of gold salt. In order to prevent a relapse, treatment was continued. Pigmentation at the site of the previous lupus erythematosus appeared after the eighth injection, or after she had received 180 mg of gold sodium thiosulfate. About this time other pigmented areas became evident on the face, particularly on the left cheek and the vermillion border of the lips. An eruption apparently due to the gold compound was first observed by the patient soon after the tenth injection, or after she had received 230 mg of the drug. Through inadvertence two additional injections were administered, in spite of them the dermatitis was not aggravated but, on the contrary,

appeared to be slowly undergoing resolution. The patient received in all twelve injections, totaling 280 mg of gold sodium thiosulfate.

The black discoloration of the skin was present for about five weeks. It was intense and evenly distributed throughout the entire area previously occupied by lupus erythematosus. In addition, a few small, various-sized pigmented areas appeared on the left cheek and a single spot on the right side of the nose, near the upper third. The vermillion border of the lips was evenly and intensely pigmented and slightly scaly. The melanosis also involved the mucous membrane of the lips, cheeks and hard and soft palate. On the mucous surface of the lips each pigmented area was discrete and the size of a pea. The blackish pigmentation was fairly intense and was symmetrically and diffusely distributed over the buccal mucosa.



Fig 2—The same patient, showing symmetrical plantar hyperkeratosis. These areas are intensely pigmented as the result of excessive production of melanin in the epidermis. (Photograph reproduced through the courtesy of Dr Howard Fox.)

and both palates. Five round whitish areas of eroded mucosa, each the size of a pinhead, likewise occurred in the mouth, two on the left cheek, one on the right, one on the lower lip and one on the gum in the region of the lower incisor teeth. The patient did not suffer from symptoms involving the mouth, such as pain, tenderness, ptyalism or a flat metallic taste. The palpebral conjunctivae were dusky and slate colored.

Dermatitis had been present for about three weeks. It was symmetrical and consisted of two types of lesions: (1) small pigmented keratotic plaques, involving chiefly the extensor surfaces of both upper and lower extremities, and (2) a diffuse pigmented hyperkeratosis, affecting both palms and soles. The keratotic plaques were roughly circular, black, firm and discrete, there was no tendency to group

or to form patches. They varied from $\frac{1}{4}$ to $\frac{1}{2}$ inch (0.64 to 1.3 cm) in diameter. Their surfaces were slightly elevated and verrucous. Intense pigmentation apparently obscured the inflammatory aspect. The lesions were not numerous, not more than a dozen were roughly scattered over each extremity. An occasional lesion was observed on the lower portion of the abdomen and on the back.



Fig 3—Low power photomicrograph of a section from a keratotic pigmented plaque of the leg. Note the thickened, adherent, hyperkeratotic scale which plugs into the dilated follicular orifices. The infiltrate is fairly dense and diffuse and is limited to the papillary and subpapillary layers of the corium. Note the lymphocytic infiltration invading the lower rete. Scattered through the infiltrate are chromatophores containing heavy deposits of melanin. Heavily pigmented melanoblasts may be seen in the suprapapillary rete and in other parts of the rete Malpighii.

The patient complained chiefly of thickened palms and soles, which felt leathery, and of some dulness of sensation in this area. The palmar and plantar surfaces were moderately and evenly thickened and were black and scaly. This feature

was most evident on the feet, but the discoloration of these areas was not as intense as that of the plaque-like lesions. The hyperkeratotic process was evenly distributed over these surfaces, there was no tendency to form irregular, verrucous projections, which are commonly observed after prolonged use of inorganic arsenical compounds. Pruritus, though present, was so mild that it did not appear to disturb the patient.

The Kahn test of the blood, the van den Bergh test and examination of the urine gave negative results. The icterus index was normal.

The patient was given intravenous injections of sodium thiosulfate, and local soothing applications were used. The ultimate result of treatment could not be ascertained, because the patient discontinued her visits to the clinic. She was under observation for these manifestations for only ten days, but during this period the eruption appeared to be undergoing gradual resolution. As might be expected, the pigmentation did not appear to be affected in the slightest by this therapy.

A section of tissue from a lesion on the outer aspect of the left leg was obtained for histologic study. The examination was made by Dr. T. J. Riordan, whose chief observations were as follows: There was present a profuse, laminated, adherent, hyperkeratotic scale, which plugged into the dilated follicular orifices. There was moderate, irregular acanthosis of the rete pegs. The pathologic process in the corium was limited to the papillary and subpapillary areas. The blood vessels were dilated. There was diffuse cellular infiltration, consisting mainly of round cells, young connective tissue cells and an occasional eosinophil. Wandering cells, mostly lymphocytes, invaded the lower rete in great numbers. Numerous chromatophores, containing heavy deposits of melanin, were scattered through the infiltrate. Small, dark deposits of melanin were noted in all layers of the epidermis.

COMMENT

There is no doubt that gold as well as arsenic is capable of stimulating the epidermal cells to proliferation and to excessive pigment formation. Pigmentation following the administration of inorganic arsenical compounds occurs only after prolonged use and is characterized clinically by a reticular or mottled appearance. Melanoderma following treatment with an organic compound of arsenic or gold appears in a comparatively short time and is distributed evenly in patches of variable size. There are, however, exceptions to this rule. Gougerot and Carteaud³ reported a case of hyperpigmentation of the reticular variety, which appeared after the resolution of gold dermatitis and which was limited to the areas previously occupied by the eruption.

Pigmentary changes merit serious consideration not only because of their tendency to persist indefinitely but also because of their disfiguring effect. The Negro race is more prone to hyperpigmentary disturbances than any other, furthermore, when such a disturbance does appear in a Negro, it is apt to be more intense than in a white person. As might be expected, melanoderma following arsphenamine therapy occurs more frequently in the Negro. It may develop on any part of the body, but it is most common on the cheek, vermilion border of the lips and buccal

3 Gougerot, H., and Carteaud, A. Pigmentation reticulée survenue après une érythrodermie aurique, *Bull. Soc. franç. de dermat. et syph.* 38: 47 (Jan.) 1931.

mucosa This reaction of the Negro skin to therapy with a gold compound unrelated to a preexisting dermatitis must be relatively rare, for it has never been previously observed in a clinic which is comprised chiefly of Negro patients This observation also applies to the development of intense melanotic pigmentation in active lesions

While it is not unusual for the arsphenamines to produce melanoderma in the Negro, they rarely cause keratoderma Except for the two cases cited of keratoderma following therapy with a gold compound, no reference to this subject has been found

In a hypersensitive person comparatively small doses may cause an unfavorable reaction In the case under discussion the cutaneous changes became evident after the patient had received only eight weekly intravenous injections of a gold salt, with an average dose of 22.5 mg

SUMMARY AND CONCLUSIONS

A case is presented in which unusual cutaneous reactions followed treatment with comparatively small doses of gold sodium thiosulfate The patient was a Negress who had suffered from chronic lupus erythematosus for one year

Melanoderma became evident after the eighth weekly injection, or after she received 180 mg of gold salt, the average dose being 22.5 mg

Keratoderma and mild stomatitis appeared after the tenth weekly injection, or after the patient received 230 mg, the average dose being 23 mg

There were no systemic evidences of hypersensitiveness to this compound

Histologic examination showed the epidermis and the papillary and subpapillary layers of the corium to be involved in the allergic reaction In the epidermis the effect was stimulating, increasing cellular proliferation and exciting the special pigment cells to an increase in activity In the corium its irritating effect manifested itself in dilatation of the blood vessels, slight edema, infiltration of round cells and proliferation of young connective tissue cells

The histologic picture was suggestive of lupus erythematosus, but the clinical appearance of the lesions and history of the case eliminated this diagnosis

It is the consensus that the allergic cutaneous reactions to gold and to arsphenamine compounds are similar in appearance A cutaneous involvement following the use of organic arsenicals is undoubtedly more frequent than that following treatment with a gold compound

The Negro race is the most susceptible to pigmentary disturbances Primary melanoderma following aurotherapy has never been observed before in this clinic in which most of the patients are Negroes

Keratoderma rarely follows therapy with a gold compound, only two similar conditions having been recorded

FUSOSPIRILLARY GANGRENOUS STOMATITIS

ELMORE B TAUBER, M D

AND

LEON GOLDMAN, M D

CINCINNATI

Ever since Richter's report in 1828 entitled "Das Wasserkrebs der Kinder," numerous reports have appeared relative to this particular syndrome. In the descriptions of many of the early cases, noma was considered as a clinical entity. This, however, is not true. It is merely a type of necrotic ulceration of selective localization and of varied etiology. Gangrenous stomatitis is only one form of noma. Rasskina-Braude and Jordan and Ryndik¹ listed the following characteristics of noma: (1) onset with ulceration of the mucous membrane, which rapidly assumes a gangrenous character and becomes grayish black, (2) edema and swelling, with central infiltration, (3) extension of the process to the adjacent skin, first with a crust and later with perforation under this crust, (4) exposure and necrosis of neighboring bones and loosening and eventual loss of teeth, (5) severe pain and a tendency to bleeding, (6) characteristic gangrenous odor, (7) secondary occurrence, (8) rapid spread of the process, with frequently a fatal end, (9) localization of the lesion not only around the mouth, but around the other orifices of the body—ears, nose, vulva, (10) debilitation, and (11) unilateral tendency of the infection.

There seems to be some difference of opinion as to the etiology. Many believe that it is caused by either a fusospirillary infection (Plaut² and Vincent³), diphtheria⁴ or a type of staphylococcus-streptococcus symbiosis. It seems that under the influence of some systemic infection or reaction the saprophytes usually present in these particular orificial areas become violently pathogenic. The condition is more common in children and occurs more frequently after measles⁵ than after the other

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1 Jordan, A., and Ryndik, R. Noma oder nomaähnliche Gangran? Arch f Dermat u Syph **169** 341, 1933.

2 Plaut, H. C. Studien zur bakteriellen Diagnostik der Diphtherie und der Anginen, Deutsche med Wchnschr **20** 920, 1894.

3 Vincent, H. Sur l'étiologie et sur les lésions anatomo-pathologiques de la pourriture d'hôpital, Ann Inst Pasteur **10** 488, 1896.

4 Repetto, E. Contributo clinico allo studio del noma, Riforma med **124** 132, 1933.

5 Vertan, E. Über einen Fall von Noma vulvae, Zentralbl f Chir **58** 2390, 1931.

contagious diseases Noma is much less frequent at the present time than it was formerly

The few reports available of the occurrence of the condition in an adult reveal evidence of systemic disturbance as a predisposing factor "Pronounced arteriosclerosis or some slight trauma, as the extraction of a tooth, may be the starting point of noma in debilitated old people" ⁶ Among the few reported cases in adults is that of Rodelius and Steyer ⁷ whose patient, a 43 year old woman, had a condition which started with gangrenous ulceration around the gum and was followed by involvement of the antrum Death occurred as a result of purulent meningitis Jedlička, Václav and Horníček ⁸ reported a case in a 35 year old woman with chronic nephritis and myocarditis, in whom noma developed after aphthous stomatitis Postmortem examination revealed gangrene of the lungs, with organisms of various types scattered throughout the tissues

The case reported here is the first observed in an adult at the Cincinnati General Hospital A few cases have been observed by the pediatric staff of the contagious service

REPORT OF A CASE

L. G., a white woman 37 years old, married, was admitted to the dermatologic service complaining of a sore in her mouth This began one month prior to her admission, with a painful ulceration underneath the tongue In spite of local treatment and three intravenous injections by her attending physicians, the lesion continued to spread Shortly before her admission, edema of the ankles and a gradually increasing effort dyspnea began to develop

When the patient was 23 years old, she was told she had "heart trouble" following rheumatism Ten years prior to her admission to the hospital, she was ill, with numerous red, tender joints, and ever since that time, she had taken active treatment for her cardiac condition There was no history, either personal or familial, of syphilis or tuberculosis

Examination on admission revealed a chronically ill white woman, who appeared very uncomfortable She was sluggish in her responses but fully oriented There was cyanosis of the lips and nail beds The skin was pale, clear and elastic General examination showed evidence of mitral stenosis, with auricular fibrillation, bilateral hydrothorax and edema of the lower extremities There was a marked fetor ex ore There were no teeth The gums were somewhat cyanotic and clear The floor of the mouth underneath the tongue was covered by a foul-smelling bluish-black necrotic area about 4 by 6 cm A slight amount of oozing occurred when any portion of the slough was removed No masses were palpable The remainder of the pharynx was clear Save for marked edema of the labia, the vaginal examination gave entirely negative results

⁶ Prinz, Hermann, and Greenbaum, Sigmund S Diseases of the Mouth and Their Treatment, Philadelphia Lea & Febiger, 1935

⁷ Rodelius, E., and St Steyer Ein Beitrag zur Frage der nomaähnlichen idiopathischen Stomatitis gangrenosa (akute Mundgangran), Beitr z klin Chir 148 476, 1930

⁸ Jedlička, V., and Horníček, V Stomatitis und Glossitis gangrenosa, Zentralbl f Haut- u Geschlechtskr 44 192, 1933

The white cell count was 8,200, with 72 per cent polymorphonuclears, 3 per cent eosinophils, 23 per cent lymphocytes and 2 per cent mononuclears. Several repetitions of this differential count showed no essential changes. The red cell count was 3,600,000, with 70 per cent hemoglobin. The urine was normal save for transient albuminuria. Smears from the floor of the mouth showed numerous fusiform bacilli and spirillas. A few cocci were also present. No diphtheria bacilli were found in culture. The Kahn reaction was negative.

The patient used neoarsphenamine in glycerin and sodium perborate locally for a few days, and at that time she took various diuretics and repeated doses of digitalis. The congestive heart failure improved rapidly. The condition in the mouth spread quickly in spite of various forms of local therapy. The administration of neoarsphenamine intravenously was started ten days after her admission, and she received a total of 3 Gm.

The local therapy consisted of sodium perborate, hydrogen peroxide, potassium permanganate, mapharsen (the hydrochloride of meta-amino-para-hydroxyphenylar-

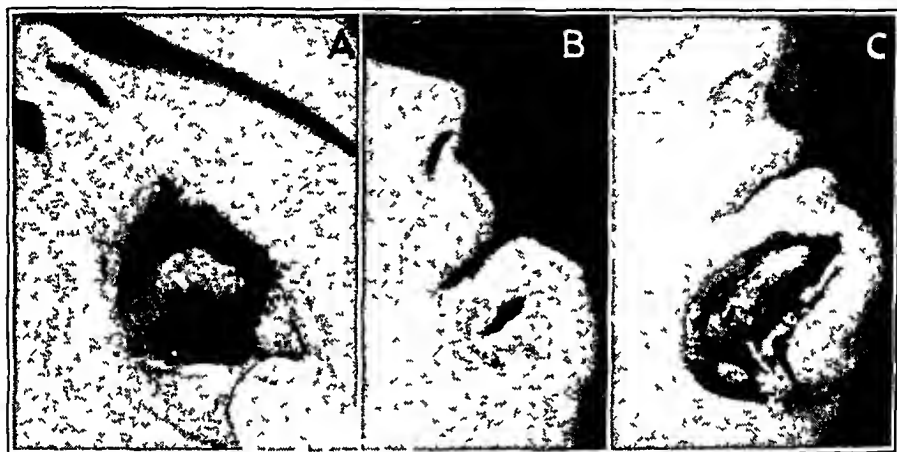


Fig 1—A, necrotic area, under the tongue at the time of the patient's admission to the hospital. B, the lesion shortly after the perforation of the gangrenous stomatitis through the chin. C, extent of the gangrenous ulceration of the tongue, the floor of the mouth and the chin shortly before death.

sine oxide), sodium ricinoleate solution, bismuth pastes and benzoyl peroxide powder. The systemic treatment, in addition to neoarsphenamine, included repeated small blood transfusions and intravenous injections of a 50 per cent solution of dextrose.

In spite of all these measures, the necrotic ulceration continued to spread, involving the entire floor of the mouth and a portion of the tongue. The mucous membrane of the lower lip was likewise involved, and overnight, perforation occurred through the lower lip. This gangrenous slough spread rapidly throughout the skin. At that time, the fusiform bacilli and spirilla were found repeatedly, both organisms in abundance. These organisms were found also on the edge of the gangrenous cutaneous slough. Culture at that time showed only hemolytic streptococci, *Bacillus coli*, staphylococci and a yeast, apparently a saprophyte. Tissue culture for a streptococcus-staphylococcus symbiosis (Dr Longacre) showed no special organisms. Bleeding from the lesion was difficult to control at times. An attempt at gentle debridement forty-eight days after admission was followed by

oozing, which could not be controlled by any local measures. In spite of various types of restoratives, the patient died ten hours after this débridement.

Postmortem examination two hours after death showed extensive endocarditis, with mitral stenosis and chronic passive congestion of the viscera, aortic and coronary atherosclerosis and hypertrophic cirrhosis of the liver. The posterior part of the pharynx showed no ulceration, and the entire tracheobronchial tree was free from ulceration. The intestines were normal. Microscopic sections of the gangrenous areas showed irregular areas of necrosis (no "three zone type") associated with polymorphonuclear and lymphocytic exudates and occasional giant cells. In the superficial portions of the ulcerated areas cocci were the only organisms identified. No spirilla were noted on smears made post mortem. Special silver stains of the tissues were not made.

COMMENT

In this patient, then, the gangrenous stomatitis developed under the influence of an old rheumatic heart disease with a recent phase of congestive failure. It is rather difficult to assign any particular systemic factor as being responsible for the development of the gangrenous stomatitis, because cirrhosis of the liver and congestive heart failure have occurred in numerous persons with dirty, infected mouths, and these patients did not acquire gangrenous stomatitis. Chronic infection of the mouth has been shown before⁹ to be an important factor in the subsequent development of severe and even fatal fusospirillary infection. In this instance, then, one can say only in a general fashion that the systemic disturbances were in favor of the development of this type of gangrene. Even after the congestive failure was relieved, the patient showed no improvement because the process had already extended too far. An attempt was made to evaluate various organisms found locally on the affected tissue, but the studies made by Dr. Longacre¹⁰ on the staphylococcus-streptococcus symbiosis showed nothing conclusive, and fusiform bacilli and spirilla were found in great abundance during the entire period of observation. In spite of the controversy concerning the fusospirillary etiology of infections of the mouth, one must say in this case that these organisms were associated constantly with the gangrenous tissue and were probably causal agents.

This case shows also the inadequacy of all forms of local and even systemic therapy. This observation was noted before⁹ in instances of fatal extensive fusospirillary infection. The question of surgical intervention, of course, is always considered, and in this case the mild attempts at débridement were responsible for hastening the inevitable death of the patient. One may generalize and say that early in the course of the disease, if the infection shows no immediate response to

9 Goldman, Leon, and Kully, Herman E. Fatal Fusospirochetal Angina, *J A M A* 101:358 (July 29) 1933.

10 Longacre, J J. Personal communication to the authors.

therapy, radical measures should be considered, since, as Jordan and Ryndik¹ claimed, "in over one half of the cases death ensues" Prinz and Greenbaum⁶ went so far as to say that "from 70 to 80 per cent of all cases end fatally in a very short time

SUMMARY

A case is reported of gangrenous stomatitis with perforation through the chin occurring in a 37 year old woman. In spite of all forms of therapy, fusiform bacilli and spirilla in great abundance were found in the tissues. The patient had also old rheumatic heart disease, with congestive failure and cirrhosis of the liver. Postmortem examination showed the localization of the gangrenous process to the buccal cavity and the chin.

PEMPHIGUS VULGARIS OF THE ERYTHEMA MULTIFORME VARIETY

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While pemphigus vulgaris is a clearly defined clinical entity, the course of the acute variety is still a matter of conjecture. In his thorough study of the subject, Riecke,¹ as late as 1931, left open the question of the nosology of the condition. Ehrmann² stated that when pemphigus is ushered in by erythema multiforme, not only is the prognosis rendered unfavorable but the course of the disease is shortened and the fatal outcome occurs sooner. In dealing with erythema multiforme bullosum, one is often baffled at the onset by inability to determine its etiology and its prognosis. The subsequent development of pemphigus is not frequent and deserves careful investigation. With these considerations in mind, we are reporting a case which presented some interesting features.

REPORT OF A CASE

L. H., a 70 year old Polish Jew, lived in the United States for thirty-seven years. Until his retirement five years previously he had been employed in the dairy business. Nothing of importance was brought to light from the family history. The patient had no knowledge of the occurrence of a bullous eruption among his relations. Except for the presence of cataracts and hemorrhoids the patient had never been sick until the present illness.

Two weeks prior to his admission to the Beth Israel Hospital, on Oct. 12, 1934, an eruption developed, it came on suddenly and, with the exception of the face, spread quickly over the whole body. It was preceded by a generalized feeling of illness, accompanied by chills, headache and nausea. The eruption consisted of urticarial lesions, which turned shortly into blisters and caused severe itching. There was no history of the ingestion of drugs. At the time of the onset of the eruption the patient was suffering from an infected toe which did not cause much discomfort and to which a salve had been applied.

Physical examination revealed an old man, in generally good condition. His hearing was slightly impaired, there was a cataract on the right eye, and the

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1 Riecke, E. Pemphigus, in Jadassohn, J. Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 7, chap. 2.

2 Ehrmann, S. Vergleichend-diagnostischer Atlas der Hautkrankheiten und der Syphilide, Jena, Gustav Fischer, 1912, p. 150.

sequelae of an iridectomy were noted in the left eye. The right pupil reacted to light and in accommodation, but the left was fixed by adhesions. The chest was emphysematous. The upper and lower extremities were swollen, though the feet were surprisingly free from edema. The heart and lungs as well as the gastrointestinal and the urogenital tract were normal.

Cutaneous examination revealed an acute inflammatory eruption, covering the entire body with the exception of the face and scalp. The lesions were vesicular and bullous. Each was situated on an inflamed base and surrounded by a hyperemic ring, they ranged in diameter from 1 to several centimeters. A fetid odor emanated from denuded areas, which were produced by the rupture of the larger bullae. The contents of the bullae, which varied according to the stage of development of the lesions, appeared at first to be clear and later seropurulent. On the toes the contents of the bullae were hemorrhagic. The mucous membranes were normal, except that there was one large bulla on the hard palate. Through coalescence of bullae on the trunk as well as on the extremities, polycyclic figures had formed. Rupture of the bullae resulted in moist areas, with tense, bulging margins. The lesions were tender on palpation.

The eruption improved gradually under local bland therapy, general hygienic measures and intramuscular injections of sodium arsenite. But the improvement was temporary, since at regular intervals a new crop of lesions with similar characteristics appeared.

In the seventh week of illness, there was a definite change in the eruption. Bullae appeared on apparently normal skin. The underlying skin showed no erythema and had lost its inflammatory character. The bullae, however, were more purulent and had a more offensive odor.

From the appearance of the eruption at this time, the diagnosis of pemphigus vulgaris was readily established. The Nikolsky sign, which had been negative at the onset, was now definitely positive. The temperature was normal.

Laboratory examination revealed that the urine had a specific gravity of 1.020 and contained numerous phosphates, a few red blood cells and a trace of albumin. The blood count showed 5,000,000 red cells and from 18,000 to 24,000 white cells per cubic millimeter. The hemoglobin content was 96 per cent (Sahli). The differential count was as follows: 85 per cent polymorphonuclear neutrophils, 10 per cent monocytes and 5 per cent eosinophils. The chemical examination of the blood revealed 33 mg of dextrose per hundred cubic centimeters. There were gram-positive and gram-negative bacilli in the feces. *Staphylococcus aureus* was observed microscopically in the contents of the bullae. The phytopharmacologic test (Pels-Macht) showed an index of 61 per cent, which indicated a highly toxic state.

During the eighth week of the disease the temperature rose to 103 F. The patient gradually became weaker, and one week later, or two and one-half months after the onset of the illness, he died of hypostatic pneumonia.

DIFFERENTIAL DIAGNOSIS

At first the diagnosis of erythema multiforme exsudativum bullosum was suggested by the following symptoms: the symmetrical arrangement of the lesions, which favored the upper and lower extremities, the bullae, which appeared on an inflamed base and were surrounded by an erythematous border, the tendency of the lesions to form configurations, and the outstanding subjective complaints. However, that diagnosis was

eliminated when we considered the course of the disease in the four weeks before the patient's death and the disappearance of the erythema, the return of the temperature to normal, the positive Nikolsky sign, the fact that the bullae arose on apparently normal skin, the large denuded cutaneous surfaces, with the offensive odor, and the lethal ending

A bullous drug eruption, such as may be produced by iodides, bromides or antipyrine, was excluded since the test of the urine for the suspected drug gave negative results and since there was no history of the ingestion of drugs. A drug eruption usually appears as a localized or as a generalized diffuse erythema, which only occasionally presents vesicular and bullous lesions and rarely causes death.

Dermatitis herpetiformis (Duhring) presents a different picture. The lesions are polymorphous and show a characteristic configuration. The general appearance of the patient is usually good, there is no fever, and the pruritus is intense. Though at times dermatitis herpetiformis closely resembles pemphigus and erythema multiforme, it can be distinguished from these by its chronic eruption, the intense itching and the history and behavior of the disease. Variola and epidermolysis bullosa acquisita were dismissed from consideration.

Pemphigus acutus infectiosus, sometimes called butcher's pemphigus, of Pernet because of the prevalence of the infection among butchers and others who deal with animals, is seen in patients who have suffered definite injury with contamination by infectious material before the outbreak of the eruption. The blebs, which develop within two weeks or a month after the injury, usually are centered around the wound. Because of its distinct features and its favorable prognosis this condition is easily recognized and can be distinguished from pemphigus.

COMMENT AND CONCLUSION

A fatal case of pemphigus vulgaris of short duration, ushered in by erythema multiforme bullosum, is described. The symptoms and the course of the eruption, with its unknown etiology, pointed to pemphigus, therefore, the following questions arose. Is there an identity of pemphigus vulgaris with erythema multiforme bullosum? Is there an actual development of a separate disease ensuing from a primary one of a different nature? Finally, is there a mutation from one disease to another? These questions will persist as long as the etiology of erythema multiforme bullosum and of kindred diseases remains unknown. The contributions to the literature supporting one hypothesis or the other are too numerous to be cited. We believe with Ehrmann that the concept of pemphigus vulgaris should be broadened to include the erythema

multiforme variant Grouven³ expressed the opinion that it is entirely plausible that the hypothetic causative agent of pemphigus vulgaris may sometimes strike suddenly and exhaust itself in a single fatal attack Pels and Macht⁴ stated the opinion that a patient with erythema multiforme bullosum who shows persistent toxicity of the blood should be regarded as having potential pemphigus Since one is unable to determine the outcome of erythema multiforme bullosum, the prognosis of this condition must be guarded

3 Grouven, C Der Pemphigus chronicus in seinen Varietaeten, Arch f Dermat u Syph 55 85, 1901

4 Pels, I R, and Macht, D I Phytopharmacologic Test in Dermatology, Arch Dermat & Syph 29 214 (Feb) 1934

FAILURE TO DEMONSTRATE SPIROCHAETA PALLIDA IN CEREBROSPINAL FLUID OF SYPH- ILITIC CHINESE PATIENTS

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AND

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The demonstration of *Spirochaeta pallida* in the cerebrospinal fluid of syphilitic patients has been successfully accomplished many times, but the frequency with which organisms may be found is still uncertain. The general impression seems to be that the incidence is comparatively high, this is probably due to the fact that positive rather than negative results have attracted attention. Few series, moreover, are sufficiently large to permit statistical evaluation of results. The matter is further complicated by the fact that various technics have been employed. At present, at least, only one, that of inoculation of animals, gives any information as to the important point of the viability of the organisms.

The majority of investigations on this aspect of syphilitic disease have been carried out on white and Negro patients in European and American clinics. In 1931 and 1932 a study was made on the cerebrospinal fluids of forty Chinese patients in Peiping by the method of inoculation of rabbits, the results of which are reported in this paper. The failure to demonstrate organisms in any of these cerebrospinal fluids is of particular interest in view of the opinion held by some observers that there are differences in the clinical manifestations of syphilis in the Occident and in the Orient.

DATA ON PATIENTS FORMING THE BASIS OF THIS STUDY

The cerebrospinal fluids of forty-two patients were studied. Forty patients were Chinese, one was an Armenian and one a Pole. Thirty-seven of the patients were males, four Chinese and the Polish patient were females. The mean age for the total series was 32 years, eight patients were 40 or more years of age, while the mean age of the others was 28. As is shown in tables 1 and 2, twenty-five patients had not been treated. With one exception, to be noted later, the amount of treatment received by seventeen patients was almost negligible. Arsphenamine, a preparation of bismuth, mercury and, occasionally, neoarsphen-

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amine were the drugs used in treatment referred to as "injection" Of seventeen patients the great majority had received but one, two or three injections at variable periods before lumbar puncture was performed In the case of two patients the intervening period was four and five days, respectively, but in that of the others it was from one month to seven years

Observations on twenty-four patients are recorded in table 1

The Wassermann reaction of the blood of all these patients was positive There were twenty-three patients with secondary syphilis of the skin and bones, in six of whom a chancre was still present, and one patient had iridocyclitis (table 1) The duration of the disease in nineteen patients was from one to eight months, in five patients it was from one to two years The duration of the symptoms ranged from ten days to six weeks in fourteen patients, in the remainder it was from two to seven months Fourteen patients had not been treated (table 1) Of the ten patients who had been treated (table 1), only one had received more than three injections, one patient had been given one injection five days before lumbar puncture was performed, but the others had not been treated for at least one month The cerebrospinal fluids of most of the twenty-four patients were normal In six fluids the cell count exceeded 4 cells per cubic millimeter, the highest counts being 10 and 12 cells, in seven the total protein content as determined by Ling's method¹ slightly exceeded 50 mg per hundred cubic centimeters, and the Wassermann reaction of one fluid was positive

Observations on eighteen patients are recorded in table 2

There were three patients with an early stage of diffuse meningitis The duration of the infection was reported to be one month, one and a half years and eight years, while the duration of the present symptoms was two weeks, one month and six months, respectively One patient had a chancre, another had a papular rash and mucous patches One patient had been given two treatments seven years previously, the others had not been treated The fluids of two patients with an early stage of diffuse meningitis showed a positive Wassermann reaction, in the fluids of all three of them the cell count was increased, and in the fluids of two the protein content was slightly increased

There were five patients with neurorecurrence affecting the eighth cranial nerve, and in one of these the second nerve was also involved (table 2) One patient had suffered from deafness (neurorecurrence) seven years before the present admission and had received thirty-seven injections of neoarsphenamine, mercury and a bismuth preparation at that time The other patients with neurorecurrence had been given from one to six treatments, one had been treated four days before lumbar puncture was made, but the others had been treated from three months to five years previously Two patients had a macular or papular rash, and a third had mucous patches The number of cells in the cerebrospinal fluids of the five patients with neurorecurrence was 5, 7, 12, 28 and 42 per cubic millimeter, respectively The total protein content of three fluids was slightly increased One fluid showed a positive Wassermann reaction, but dark-field examination of a centrifugated portion of that fluid gave negative results

Of five patients with tertiary syphilis (table 2) one had aortic insufficiency, one, aortic aneurysm, one, cutaneous gumma and periostitis, one, keratitis and bursitis, and one, periostitis and alopecia In these patients the duration of the disease was reported as ranging from four to twenty years, and that of the present symptoms, from three months to three years Only one patient had been treated, and the treatment had consisted of a single injection given one month

1. Ling, S M J Biol Chem 69 397, 1926

TABLE 1—Observations on Patients not Showing Evidence of the Nervous System

Case Num ber	Duration of Disease	Symptoms	Treatment		Observations on Cerebrospinal Fluid			First Animal Passage		Second Animal Passage			
			Period of Hospi- taliza- tion	Number of Injec- tions	Time Be- tween Last Injection and Lumbar Puncture	Was ser mann Reac- tion	Number of Cells per Cumm	Total Protein Content, Mg per 100 Cc	Number of Rabbits	Number of Exam- inations	Interval Between Inocu- lations, Days	Number of Rabbits	Number of Exam- inations, Days
1	1 mo	Papular rash, chancre	1 wk	None	—	—	54	2	7	61-132	4	7	83-150
2	2 mo	Papular rash, chancre	2 wk	None	—	3	+	1	4	86	1	2	121
3	1 mo	Macular rash, chancre	10 days	None	—	3	+	1	5	94	2	4	127
4	2 mo	Macular rash, chancre	?	None	—	10	?	2	3	87	2	2	98 123
5	?	Macular rash, chancre, arrhythmia	?	None	—	5	?	2	2	79	2		188
6	2 mo	Papular rash	2 wk	None	—	2	5 [†]	2	3	93	1		123
7	?	Papular rash, arrhythmia	6 wk	None	—	—	—	2	3	94	2	1	204
8	?	Papular rash, headache, arrhythmia	7 wk	None	—	2	+	2	3	85	2	2	132
9	2 mo	Papular rash	12 days	None	—	2	—	2	3	98	2	2	212
10	2 yr	Follicular rash	5 mo	None	—	6	+	2	2	100			
11	1 mo	Condyloma	6 wk	None	—	—	—	2	2	77	2		170
12	8 mo	Condyloma	2 wk	None	—	*	?	1	3	82	2	1	182
13	1 yr	Condyloma, alopecia	4 wk	None	—	—	51	2	2	104			
14	?	Condyloma	2 wk	None	—	6	—	2	1	114	2		180
15	18 mo ?	Periostitis, chancre	2 mo	2	2 mo	+	?	2	3	102	2	2	108 188
16	1 mo	Papular rash	2 wk	1	5 days	—	3	60	2	79	2		188
17	2 yr	Condylomas	2 mo	1	2 yr	—	8*	+	2	84	2	3	130
18	?	Condylomas	2 mo	3	1 yr	—	8	50	2	105	2		45-50
19	11 mo	Papular rash, Periostitis	2 wk	7	4 mo	—	4	—	1	100	2	1	108
20	2 yr	Periostitis	7 mo	2	2 yr	—	3	52	1	119	2	—	104
21	1 mo	Papular rash, alopecia	2 wk	3	1 mo	—	1	40	2	86 165	1	4	135
22	1 mo	Condylomas, alopecia	6 wk	1	4 mo	—	2	36	2	82	2	4	136
23	7 mo	Iridocyclitis	1 wk	2	7 mo	—	12	48	2	204	2		130
24	?	Periostitis	4 mo	1	1 mo	—	2	—	3	83	2	1	185

* The fluid was blood tinged

† This patient was a Pole

TABLE 2.—Observations on Patients with Involvement of the Nervous System or with Tertiary or with Latent Stages of Syphilis

Case Num ber	Duration of Disease	Symptoms	Treatment		Observations on Cerebrospinal Fluid			First Animal Passage			Second Animal Passage		
			Number of Injec tions	Time Be tween Last Injection and Lumbar Puncture	Was ser mann Reac tion	Number of Cells per Cu mm	Total Protein Content, Mg per 100 Ce	Number of Blood Rabbits	Number of E-mi nations	Interval Between Inocu lations, Days	Number of Blood Rabbits	Number of E-mi nations	Period of Obser vation, Days
				Early Stage of Diffuse Meningitis									
25	1 mo	Headache, chancre	None		—	35	52	2	6	88	2	1	174
26	18 mo	Headache, papular rash, macular patches	None		+	+	50	2	6	102	2	2	188
27	8 yr ?	Headache	2	7 yr	+	700	?	1	3	100	2	1	170
28	4 mo	Involvement of 8th cranial nerve, macular patches	1	3 mo	—	12	52	2		68	2		170
29	?	Involvement of 8th cranial nerve	6	4 days	—	5	56	2	3	81	2	1	127 185
30	4 mo	Involvement of the 8th and 2d cranial nerves	2	3 mo	+	7	+	1	2	85	2		188
31	3 yr	Involvement of 8th cranial nerve, papular rash, con dytomas	1	3 yr	—	28	52	2	1	74	2		170
32	8 yr	Involvement of 8th cranial nerve, macular rash, ar rhythmia	37	5 yr	—	42	49	2	1	125	2		100
33	4 yr ?	Aortic insufficiency	None		—	3	51	2	2	94	2	1	105
34	20 yr	Aortic aneurysm	None		—	2	+	2	1	119	2		104
35	13 yr	Cutaneous gumma, perlos titis (2 wk)	None		—	4	52	2	2	70	2		173
36	7 yr	Keratitis, bursitis (3 mo)	None		—	2	47	2	1	70	2		170
37	24 yr	Periostitis, alopecia	1	1 mo	—	4	55	2	3	83	2	1	186
38	7 yr		None		—	2	51	1	2	83	2	1	182
39	12 yr ?		None		—	2	?	2	8	89	2	2	113 133
40	6 yr		None		—	—	53	2	1	103	2		104
41	12 yr	Diminished reflexes	None		+	70	56	2	5	95	1	1	174
42†	20 yr	Asymptomatic involve ment of the central ner vous system	None		+	642	++	2	2	107	2		104

* The fluid was blood tinged

† This patient was an Armenian

previously. The spinal fluids of all the patients with tertiary syphilis were normal except for the fact that three specimens showed slightly high values for the total protein content.

The last group of five patients (table 2) comprised three with latent syphilis, one with questionable tabes and one with asymptomatic neurosyphilis. The duration of disease was from six to twenty years. None of them had been treated. The spinal fluids of the patients with latent syphilis were practically normal. The fluids of the other two showed a positive Wassermann reaction, an increased cell count and an increased value for the total protein content. The colloidal gold curve and the mastic curve of the fluid of the patient with questionable tabes were normal.

EXPERIMENTAL PROCEDURE

Within a few minutes after the fluid was withdrawn, each of the forty-two fluids, without being centrifugated, was injected into one or both of the testicles of normal adult rabbits. Each of thirty-five fluids was tested on two rabbits and each of seven fluids, on one rabbit, a total of seventy-seven animals being used. The amount of fluid available after the removal of a portion for other tests determined whether one or two animals were used. In the majority of cases from 1 to 2 cc was injected into each animal, a few received 0.75 cc. The rabbits were kept under observation for an average of three and one-third months, the majority being observed for at least three months, the longest period of observation was two hundred and four days and the shortest sixty-eight days.

A second animal passage was carried out in forty cases, that is, the test was repeated with material derived from the rabbits which had received forty of the forty-two fluids.

The mean interval before the second passage was three months after the injection for the first passage. The longest interval was one hundred and twenty-five and the shortest sixty-one days, respectively, in only seven cases was the interval less than eighty days. The material used for inoculation was an emulsion of both popliteal lymph nodes in saline solution, nodes from both or from only one of the originally inoculated animals being used. For ten transfers the nodes were removed surgically with the animal under ether anesthesia, and the rabbit was kept under observation for a variable period thereafter. For thirty transfers the rabbit was killed by an injection of air into a marginal vein of the ear, and the nodes were removed aseptically. A small amount of a comparatively thick emulsion was prepared so that all the material from the nodes could be used. In three instances portions of the originally inoculated testicle were included in the emulsion. The inoculations were made intratesticularly in normal rabbits, the average dose for each animal being 1 cc.

For the second animal passage a total of seventy-eight rabbits received injections, thirty-five emulsions being tested on two, four on one and one on four rabbits. The animals were observed for a mean interval of one hundred and seventy days, seventy-five were followed for from one hundred to two hundred and four days, while three were observed for forty-five, fifty and eighty-three days, respectively.

In one instance a third animal passage was carried out. The popliteal lymph nodes of two rabbits used for the second passage were removed one hundred and four days after the animals had been inoculated. The emulsion was injected intratesticularly in two normal rabbits which were observed for one hundred days.

All the rabbits were carefully examined clinically at least twice a week for local and general evidence of infection. Examination always included palpation of the testicles, whether inoculated or not, and of the popliteal lymph nodes. In

instances in which the presence of pathologic changes in the testicles was suspected, aspirated testicular fluid was examined microscopically by the dark-field method

Wassermann, Kahn and Kline tests were made on the blood serums of the majority of the rabbits. In ascertaining the results of the first passage, these tests were made on the serums of the animals inoculated with thirty-eight of the forty-two fluids. The number of examinations of the blood per set of animals representing each fluid varied from one to eight, the average being three examinations. In determining the results of the second passage tests were carried out on twenty-three of the forty sets of inoculated rabbits. From one to seven tests were made, the average being two tests on each set of rabbits.

At the end of the period of observation each rabbit was killed by an intravenous injection of air. At postmortem examination particular attention was paid to the testicular and lymphatic tissues, and in many cases a dark-field examination of testicular fluid was made. The tissues were not studied histologically.

RESULTS

The results of this large series of experiments with the cerebrospinal fluids of forty-two patients with various stages of syphilis were uniformly negative. The total number of rabbits studied was one hundred and fifty-seven. Seventy-seven rabbits received injections of spinal fluids (first animal passage), seventy-eight received injections of emulsions of the popliteal lymph nodes obtained from the originally inoculated animals (second animal passage), and two rabbits received injections of emulsions of the popliteal lymph nodes of two rabbits used for the second passage, representing a third animal passage. In a considerable number of instances it was thought that the testicle into which infective material had been injected had undergone slight changes, consisting chiefly of formation of small areas of thickening or induration, but in no case did the condition progress or persist. Dark-field examination of testicular fluid aspirated in these instances gave negative results.

The results of the Wassermann, Kahn and Kline tests of the blood serum of the rabbits were likewise negative. There were some examples of a "weakly positive" result, and an occasional specimen of serum was reported to show a "positive" reaction to one of the tests, but in no instance were all three tests of the same specimen positive and in none did the positive reaction persist.

COMMENT

Of the various technics employed for the demonstration of organisms in the cerebrospinal fluid of syphilitic patients, that of inoculation of rabbits has been increasingly employed (1) because by this method spirochetes have been demonstrated in fluids considered to be normal by the usual tests, (2) because it furnishes information as to the viability of the spirochetes, and (3) because it is simple. The histologic method of Warthin and Wile carried out on stained specimens of

artificially prepared spinal fluid clot and the direct method of dark-field examination of the fluid obviously give no information as to the viability of the organism. This histologic method, furthermore, requires extended experience before reliable results are assured.

By means of inoculation of rabbits viable spirochetes have been successfully demonstrated in a considerable number of fluids. As based on experiments made in the early stage of the disease, at the time of general dissemination of organisms, the results of various workers have been in general agreement. Chesney and Kemp² reported that spirochetes were demonstrated in five, or 14.7 per cent, of the fluids of thirty-four patients with early stages of secondary syphilis who had normal spinal fluids. As these authors pointed out, similar results were obtained in three other series of comparable cases. Thus, positive results were obtained in three, or 15 per cent, of twenty cases studied by Steiner,³ two, or 18.8 per cent, of eleven cases reported by Arzt and Kerl,⁴ and in two, or 20 per cent, of the ten cases observed by Fruhwald and Zaloziecki.⁵

In later stages of the disease a number of successful results have been reported, but there are not sufficient available data to enable one to say what is the incidence of viable organisms in the fluid. There is undoubtedly great variability in individual patients, even in the case of those with involvement of the central nervous system, with respect both to the occurrence and to the persistence of organisms in the spinal fluid. In Steiner's³ nineteen cases of neurosyphilis, the results of inoculation of rabbits were negative. Arzt and Kerl⁴ reported successful results in two of six cases of dementia paralytica and in two of three cases of tabes, in two cases of cerebral syphilis the experiments were unsuccessful. In Wile's⁶ eight cases, testicular inoculation of rabbits gave a high incidence of positive results, that is, spirochetes were found in the fluid in two of three cases of dementia paralytica, in one of three cases of tabes, in the one case of neurorecurrence investigated and in the one case of asymptomatic syphilis of the central nervous system. Fruhwald and Zaloziecki's⁵ series contained one case of a late stage of syphilis (cutaneous gumma) and three cases in which symptoms of involvement of the central nervous system were present, the single positive result was obtained in one of the cases of a later stage of the

2 Chesney, A. M., and Kemp, J. E. Incidence of *Spirochaeta Pallida* in Cerebrospinal Fluid During Early Stages of Syphilis, *J. A. M. A.* **83** 1725 (Nov. 29) 1924.

3 Steiner, G. *Neurol. Centralbl.* **33**:132, 1914.

4 Arzt, L., and Kerl, W. *Wien klin. Wchnschr.* **27** 785, 1914.

5 Fruhwald, R., and Zaloziecki, A. *Berl. klin. Wchnschr.* **53**:9, 1916.

6 Wile, U. J. *Am. J. Syph.* **1**:84, 1917.

disease in which progressive paralysis was present Nichols and Hough,⁷ Reasoner,⁸ Kemp and Chesney⁹ and McIntosh and Michelson¹⁰ were successful in demonstrating viable organisms in the cerebrospinal fluid in individual cases by inoculation of rabbits Volk¹¹ also obtained a positive reaction with spinal fluid from a paralytic patient, in four other cases in which the type of disease is not mentioned, the results were negative

Judging from these findings, it might be expected that from among the twenty-three of our patients with early stages of the disease, that is, fourteen patients with untreated early stages of syphilis (table 1), six with early stages of the disease who had received one or two treatments at least two months before the time of the observations (table 1) and three with early stages of diffuse meningitis (table 2), there would have been three or four positive results Similarly, among four patients with neurorecurrence (table 2) not treated for from three months to five years, one positive result might have been expected With respect to the patients with tertiary and latent syphilis negative results might probably have been predicted The marked changes in the cerebrospinal fluid in the case of the Armenian patient with asymptomatic involvement of the nervous system may or may not have been associated with the presence of organisms

The period of incubation of the induced infection in rabbits as reported by the aforementioned investigators was variable As short a time as from four to seventeen days was reported by Wile, and longer periods (four months) were observed by Steiner and Volk, but in the majority of cases the period was from one and a half to three months It should be particularly noted that in two of Chesney and Kemp's five cases in which successful results were obtained with fluids from patients with early stages of untreated secondary syphilis, positive results were not seen in the animals used for the first passage but were obtained in rabbits inoculated with emulsions of tissue from the popliteal lymph nodes and testes of the animals originally inoculated (second animals passage)

With forty of the forty-two fluids forming the basis of the present study a second animal passage was carried out Furthermore, the period of observation was comparable to that in successful experiments reported

7 Nichols, H J, and Hough, W H Demonstration of *Spirochaeta Pallida* in the Cerebrospinal Fluid, *J A M A* 60 108 (Jan 11) 1913

8 Reasoner, M A Some Phases of Experimental Syphilis, *J A M A* 67 1799 (Dec 16) 1916

9 Kemp, J E, and Chesney, A M *Bull Johns Hopkins Hosp* 36 199, 1925

10 McIntosh, J A, and Michelson, I D *Memphis M J* 5 9, 1928

11 Volk, R *Wien klin Wchnschr* 26 1824, 1913

by other workers. The one hundred and fifty-seven rabbits inoculated were, with two exceptions, observed for more than two months, and these two animals were observed for forty-five and fifty days, respectively. The great majority, that is, one hundred and thirty-two animals, or 85 per cent, were under observation for three months or longer.

The choice of tissue from the popliteal lymph nodes for the inoculum for the second animal passage was based on the well known predilection of *S. pallida* for lymphoid tissue in experimental syphilis of the rabbit. The systemic infection includes involvement of the lymph nodes, and viable organisms have been recovered from the popliteal nodes in cases of latent syphilis of long standing¹². It is theoretically possible that infection might occur without evident testicular reaction in the case of a spinal fluid containing small numbers of organisms or organisms of a low degree of virulence, but it was thought that the best chances of recovering organisms in such circumstances lay in the use of the popliteal lymph nodes.

An interesting feature of Chesney and Kemp's results, which were obtained with normal spinal fluids of patients with early stages of untreated syphilis, was that in four of their five cases in which demonstration of spirochetes was successful the patients were females. There were sixteen females and eighteen males in their series, the incidence of positive results being 25 per cent for the females and 5.5 per cent for the males. Our patients were, with five exceptions, males. Analysis of Chesney and Kemp's results by the chi-square test of homogeneity,¹³ however, shows that the difference in incidence of their positive results between the two sexes is not statistically significant (chi-square = 2.406, $p = 0.01$). That is, the chances of obtaining a positive result were not better with the spinal fluids of their female patients than with those of their male patients.

There are three features in which our material differs from that of others who have been successful in demonstrating spirochetes in the spinal fluid of syphilitic patients. The first concerns the organism involved. As far as is known—and it is certainly reasonable to presume that such was the case—the infection in all our patients could be attributed to an organism of Oriental source. The question whether such strains differ in their biologic characteristics from strains obtained from Occidental sources was investigated in a series of experiments on rabbits carried out in Peiping and in New York¹⁴. The results of this work

12 Pearce, L., and Brown, W. H. *J. Exper. Med.* **35**:39, 1922.

13 Fisher, R. A. *Statistical Methods for Research Workers*, London, Oliver & Boyd, 1930.

14 Pearce, L. Unpublished data.

indicate that as far as the reaction of the rabbit was concerned, the essential pathogenic properties of the Oriental and those of the Occidental strains which were studied were similar

The second difference is that our inoculations were made in native albino rabbits obtained in Peiping while those of other workers were made in American and European rabbits. It is known that breed may have a definite influence on the course of experimental syphilis in the rabbit,¹⁵ and extensive experience with a rabbit-breeding colony has shown that the factor of breed is significantly associated with the host's reaction to a variety of conditions. In the present instance, however, it does not appear probable that the use of Chinese rabbits could be the sole reason for the uniformly negative results obtained. The comparative experiments just referred to included the use of both Chinese and American rabbits, and in every instance intratesticular inoculation induced a well marked orchitis. In certain respects the pathologic picture appeared to be influenced by the particular breed of animal used, but the findings did not suggest such a level of insusceptibility or resistance as to bring about completely negative results.

The third difference is that of race, the majority of our patients being Chinese while those of other workers were white persons or Negroes observed in Europe and America. So far as the clinical manifestations were concerned, those observed in our patients did not differ from those exhibited by patients in the Occident. The opinion has been expressed, however, that syphilis in the Orient differs from that in the Occident chiefly with respect to a lower incidence of involvement of the central nervous system. Physicians with extensive clinical experience in Oriental countries report comparatively few cases of locomotor ataxia or dementia paralytica in native patients, in contrast to the expected incidence of such conditions in their white patients. Furthermore, the reaction to syphilis of Negroes differs in many respects from that of white patients, as has been shown by several observers, notably by those at the Johns Hopkins Hospital.¹⁶ That Chinese patients may also present peculiarities or differences of reaction is entirely possible, and the results of this study may be an instance in point.

It is known that the presence of viable organisms is not necessarily associated with cellular and other abnormalities of the fluid, while the recovery of organisms from abnormal fluids appears to be unpredictable. In the light of the uniformly negative results obtained on a mixed series of forty patients with a technic which gave ample opportunity for the recovery of viable organisms, it appears either that the true incidence of viable *S. pallida* in the spinal fluids of syphilitic patients is not as

15 Rosahn, P. D. *J. Exper. Med.* 57: 907, 1933.

16 Turner, T. B. *Bull. Johns Hopkins Hosp.* 46: 159, 1930.

high as has been thought or that the reaction of Chinese patients to *S pallida* is of such an order that viable organisms either find their way less frequently into the cerebrospinal fluid or do not persist there as long as appears to be the case in patients of other races. Perhaps both explanations are applicable. Until the results in other series are available, however, the present observations may be tentatively interpreted on the basis of differences or peculiarities in the racial character of the reaction to syphilitic infection.

CONCLUSION

The attempt to demonstrate *S pallida* in the cerebrospinal fluids of forty Chinese and two European syphilitic patients by means of inoculation of rabbits was uniformly unsuccessful.

EVALUATION OF THE PHYTOPHARMACOLOGIC TEST OF PELS AND MACHT

FURTHER REPORT

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The phytopharmacologic test devised by Pels and Macht¹ for determining the toxicity of the blood serums of patients with anemia and various diseases has been applied by us. In some cases modifications of the tests were attempted. A summary of this work is reported.

The technic of the test has already been published several times by the originators. It consists in measuring the amount of retardation of the growth of rootlets in a plant nutrient solution to which has been added a small percentage of a patient's blood serum. The modifications used in our laboratory are as follows:

1 Not only a solution containing 1 per cent but also solutions containing 5, 10, 25 and 33 per cent serum were used.

2 It was found² that seedlings of *Zea mays* (popcorn) responded similarly to those of *Lupinus* when exposed to a test solution. Other plants used in these tests were *Raphanus* (radish), *Fagopyrum* (buckwheat), *Allium* (onion) and *Salix* (swamp-willow cuttings with sprouted rootlets).³

3 In addition to the tests consisting of the first twenty-four hour immersion in a plant nutrient solution containing serum (reading A) measurements were made after a second twenty-four hour period of growth of the same seedlings in a normal plant nutrient (Shive)⁴ solution (reading B).

From the Pittsburgh Skin and Cancer Foundation

1 Pels, I R, and Macht, D I. Phytopharmacology of Pemphigus and Other Dermatoses. Additional Studies, *Arch Dermat & Syph* **23** 601 (April) 1931

2 Hollander, Lester, and Greb, Raymond J. Evaluation of the Phytopharmacologic Test of Pels and Macht, *Arch Dermat & Syph* **33** 1012 (June) 1936

3 Greb, Raymond J. Various Plants in the Phytopharmacological Test, *Proc Pennsylvania Acad Sc* **9** 98, 1935

4 Shive, J H. A Study of Physiological Balance in Nutrient Media, *Physiol Researches* **1** 327, 1915

PRESENTATION OF DATA

The data presented here have been summarized and grouped in the following manner (a) according to diseases, (b) according to plants used, (c) according to the percentage of serum in the nutrient solution (test solution) and (d) according to sex when enough similar tests were made to permit grouping in this manner. No summaries according to age were attempted since it was obvious that extreme variation occurs regardless of age, and, moreover, the ages of the persons tested were too distantly separated to permit grouping.

Syphilis—Serums from thirty-one patients receiving antisiphilic treatments were tested. The averages recorded were extremely variable in the different cases. Results from eighteen serums tested with *Raphanus* in a solution containing 5 per cent serum ranged from a low average of 0.58 mm to a high of 4.68 mm for reading A. The grand average of growth established for this group from the aforementioned eighteen serums was 2.95 mm. The average number of plants used in each test was 18. The ten serums tested with *Lupinus* under similar conditions gave a grand average of 3.31 mm, 27 plants being the average number used in each test reading A (table 1). Plants used in the aforementioned ten tests when measured after the second immersion (reading B) gave a grand average of 6.93 mm.

A few tests were made with *Zea mays* and *Fagopyrum*, but the data are too limited for presentation.

When the foregoing data were grouped according to sex, thirteen tests with *Raphanus* made on serums from male patients showed an average growth of 3.37 mm and five tests on serums from female patients gave an average growth of 1.90 mm. With *Lupinus*, tests of six serums from males gave an average reading of 2.99 mm, and those of four serums from females gave an average of 3.99 mm.

Pemphigus—Thirteen tests were made on the serums of six patients with pemphigus. Five tests were made with *Lupinus* in a solution containing 5 per cent serum. The grand average for serums from patients with pemphigus (reading A) was 3.84 mm, 31 seedlings for each test. Four of the groups of test plants measured after the second immersion (reading B) showed an average growth of 9.39 mm.

The grand average for the four tests with solution containing 1 per cent serum was 7.75 mm, an average of 39 seedlings being used for each test. When three of these four test plants were exposed to the second immersion (reading B) the average growth was 10.79 mm.

Seedlings of *Zea mays* in a solution containing 1 per cent serum gave a grand average of 4.73 mm for six tests (reading A). The average number of seedlings used for each test was 53. Four of these seedlings when exposed to the second immersion (reading B) showed a grand average of 10.68 mm.

Records of other tests with *Zea mays* in solution containing 5 per cent serum as well as with other plants in various solutions are too meager to consider here.

The average results of tests on the serum from one female patient (case 163) with *Lupinus* in a solution containing 1 per cent serum ranged from 13.27 to 5.62 mm after forty days. This patient was receiving treatment for active pemphigus. About eighty days later, a solution containing 1 per cent of her serum elicited a

TABLE 1—Summary of Averages with *Lupinus* as the Test Plant

Condition of Patient	1 per Cent Solution Reading A, Grand Average, Mm	Number of Serums Tested	Average Number of Plants Used	Lowest Average, Mm	Highest Average, Mm	Reading B, Grand Average, Mm	Number of Serums Tested	Average Number of Plants Used	Lowest Average, Mm	Highest Average, Mm	Reading B, Grand Average, Mm	Number of Serums Tested	Lowest Average, Mm	Highest Average, Mm
Syphilis	4 70	2	20	3 40	6 00	7 43	2	20	3 40	6 00	7 43	2	3 40	6 00
Gonorrhoic	7 75	4	39	5 62	13 27	10 79	3	39	5 62	13 27	10 79	3	5 62	13 27
Gonorrhoic anemla	5 75	10	48	3 35	7 84	9 47	8	48	3 35	7 84	9 47	8	3 35	7 84
Miscellaneous dermatitis	6 56	8	61	3 10	10 70	8 85	7	61	3 10	10 70	8 85	7	3 10	10 70
Cancer of breast														
Cancer of lip														
Cancer of cervix														
Lymphosarcoma														
Miscellaneous cancers	7 12	4	50	4 84	9 41	9 97	3	50	4 84	9 41	9 97	3	4 84	9 41
Normal	6 54	7	45	4 52	11 24			45	4 52	11 24			4 52	11 24

TABLE 2.—Summary of Averages with Zea Mays as the Test Plant

[illegible]

growth of 632 mm Recently serum from one male patient (case 200) presenting an advanced stage of treated pemphigus gave a reading of 581 mm (reading A) with *Lupinus* in solution containing 1 per cent serum

Anemia and Leukemia—There were seventeen tests with blood serums from fifteen patients having some form of pernicious anemia, secondary anemia or lymphatic leukemia In most of these tests both *Lupinus* and *Zea mays* as well as various concentrations of the serums were used

Ten serums tested with *Lupinus* in solution containing 1 per cent serum produced an average of 575 mm (reading A) The average number of seedlings used in each test was 48 (table 1) In the second series of tests nine of these ten serums produced an average of 947 mm (reading B)

Reading A on *Lupinus* in a solution containing 5 per cent serum (table 1) showed an average growth of 214 mm for seven serums tested, an average of 24 seedlings per test being used Reading B on plants tested with the seven serums averaged 715 mm

Eight serums tested with *Zea mays* (table 2) in a solution containing 1 per cent serum showed an average growth of 421 mm Forty-seven seedlings were used in each test on the average Reading B on plants tested with these serums showed an average growth of 912 mm

An average of 206 mm (reading A) was established for five serums with *Zea mays* (table 2) in solution containing 5 per cent serum The average number of seedlings used in these tests was 19 Reading B showed 1016 mm as a grand average

Reading A on plants tested with solution containing 1 per cent serum, the serums being grouped according to the patient's sex, showed the following results With *Lupinus* four tests on serums from male patients showed an average growth of 579 mm, six tests on serums from female patients gave an average growth of 574 mm With *Zea mays* six tests on serums from females showed an average growth of 417 mm, and an average growth of 431 mm was obtained from two tests on serums from males Readings for the solution containing 5 per cent serum were similarly variable

Miscellaneous Dermatoses—Under this heading are grouped such disorders as pruritus, epidermolysis, erythema, acne and scabies The same degree of variation was noted between results of tests on serums from patients with these diseases as between those of tests on serums from anemic, syphilitic and normal persons Eight serums tested with *Lupinus* in solution containing 1 per cent serum (table 1) elicited the following readings reading A, grand average, 656 mm, 61 seedlings in each test, reading B, grand average, 885 mm Eight serums tested in solution containing 5 per cent serum gave the following results reading A, grand average 349 mm (average number of seedlings, 22), reading B, grand average 922 mm

Only three serums were tested with *Zea mays* in solution containing 1 per cent serum The following averages were obtained reading A, grand average, 505 mm (24 seedlings), reading B, grand average 846 mm Three serums tested by means of solution containing 5 per cent serum gave results as follows reading A, grand average 226 mm (14 seedlings), reading B, grand average 1040 mm

Malignant Conditions—Serums from fifty-two patients with carcinoma of various organs were tested This series comprised (a) ten patients with carcinoma of the breast, (b) eight with carcinoma of the lip, (c) eight with carcinoma of the cervix, (d) five with lymphosarcoma and (e) twenty-one with carcinoma involving some part of the body other than those listed

Serums from seven of the patients with carcinoma of the breast were tested with *Lupinus* in solution containing 5 per cent serum (table 1). An average growth of 3.56 mm (reading A) was obtained. Eighteen seedlings on the average were used in each test. Reading B showed a grand average of 6.7 mm.

Six tests with *Zea mays* (table 2) in solution containing 5 per cent serum showed an average growth of 3.19 mm, an average of 18 seedlings being used in each test. Reading B for this group averaged 5.94 mm.

Serums from patients with carcinoma of the lip gave about the same results. Six serums were tested with *Lupinus* (table 1) in solution containing 5 per cent serum. These gave an average of 3.58 mm (reading A) with 18 plants for each test. Reading B showed an average of 8.39 mm.

Zea mays in solution containing 5 per cent serum (table 2) showed an average growth of 3.50 mm in five tests, 24 plants being used for each test, reading B showed an average growth of 7.99 mm.

Readings obtained for the patients with other types of tumors showed similar variation. Average readings are listed in tables 1 and 2.

Observations on Serum from "Normal" Persons—A summary of the tests in which serums from "normal" persons (persons with no demonstrable disease) were used shows the following averages. Twenty-two serums tested with *Lupinus* in solution containing 5 per cent serum (table 1) gave an average reading of 3.10 mm of growth with an average of 17 seedlings per test. Reading B on eighteen tests showed an average of 7.25 mm.

Seven serums were tested by means of solutions containing 1 per cent serum. The average obtained from these was 6.54 mm, *Lupinus* being used. The average number of seedlings was 45.

With *Zea mays* (table 2) the following averages were obtained in solutions containing 5 per cent serum. Reading A, grand average for seven serums 3.57 mm (average number of seedlings, 32), reading B, grand average 10.70 for six tests.

Plant Nutrient Solutions Only—*Lupinus* grown in the plant nutrient solution gave an average of only 9.79 mm for the 586 plants tested. This figure may be used as the basis for comparison in estimating the phytotoxic index of any one serum. *Zea mays* grown under the same conditions showed an average growth of 9.86 mm for the 317 plants tested.

COMMENT

From the data now available in this laboratory it seems obvious that the encouraging results obtained by Macht and his co-workers in their work on pernicious anemia and pemphigus vulgaris were not duplicated here.

While it may be maintained that the data here presented do show a low phytotoxic index in some cases of both pernicious anemia and pemphigus vulgaris, there are also many nonconformist cases. An index of over 130 in a case of suspected, and later proved, pemphigus (case 163) indicates that the test is unreliable. The extremely low indexes that are most difficult to explain on the basis of specific toxicity, however, are those obtained from the tests on serums from "normal" persons as well as on those from patients with conditions listed under

carcinoma, syphilis, etc. In all the latter groups the readings should be above any obtained with serums from patients with pemphigus or anemia, according to the evidence presented by Macht and his co-workers. In the data shown in tables 1 and 2, indexes as low as any obtained with serums from patients with either anemia or pemphigus may be noted.

The variations observed when the plants were immersed for a second twenty-four hour period in a plant nutrient solution to which no serum had been added further substantiate the weakness of the phytopharmacologic tests. All the plants immersed in a solution containing serum showed a subsequent effect when observed for a second twenty-four hour period. No uniform result was obtained during this period after any of the tests on serums, as recorded in table 1. The same incongruous variations are shown in table 2. In some instances, when the retardation of growth was great during the first twenty-four hour period, the amount of growth obtained during the second twenty-four hour period was also low. Many exceptions may be noted from table 1.

SUMMARY AND CONCLUSIONS

No uniformity of growth could be obtained with any of the series of serums from patients with the diseases tested.

The readings obtained for serums from patients with pernicious anemia or pemphigus vulgaris show variations as low as do readings for serums from patients with carcinoma or syphilis or for serums from normal persons.

Many of the variable results obtained may be ascribed to differences in individual growth potentials of seedlings.

A genetically homozygous strain of plant rootlets must be developed. This would reduce growth potential differences.

As was previously pointed out,² in order to get a reliable measure of toxicity the number of plants exposed to a test must be great enough to insure a statistically sound mean of growth. Such a test becomes a real time-consuming problem, and since, at best, the test seems to be of doubtful value as a diagnostic measure, some modification of the technic, such as producing a strain of seedlings genetically uniform in their root growth potential,³ must be developed.

XERODERMA PIGMENTOSUM

AN INHERITED DISEASE DUE TO RECESSIVE DETERMINERS

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Despite the rapid growth of genetics in the last quarter of a century, there is little in the modern medical textbooks to indicate the applications of genetics to medicine. Statements that are obviously incorrect with respect to the inheritance of disease still find a place in modern textbooks. To some extent this is true of the rare condition of xeroderma pigmentosum. Although it was early recognized that this disease is in part dependent on a constitutional factor, it is not generally conceded that this factor is inherited. Thus, one still finds the statement that xeroderma pigmentosum is not hereditary but "familial." In the 1927 edition of his textbook on diseases of the skin Sequeira stated "It does not appear to be hereditary, the fact that the patients rarely survive puberty probably explaining this." This mistaken idea is due, as will shortly be seen, to a misunderstanding of what is meant by the term hereditary.

There are other erroneous statements in the literature on this disease, and, as will be shown later, they are all made because of inadequate understanding of the operation of the laws of inheritance. Thus, although it is not generally conceded that xeroderma pigmentosum is hereditary, the statement is frequently encountered that more than one child in the family is usually affected. Hence, the disease is called familial. I shall point out that the disease is hereditary but that, in spite of this, because of the nature of its transmission, only one child is affected in the majority of families. This statement may sound paradoxical, but it is easily comprehended when the laws of inheritance are understood.

Another mistaken idea is that, although in the aggregate males and females are equally affected, only one sex is involved in any one family—that is, one family has only sons affected and another only daughters, but as a rule both sexes are not affected in the same family. If the disease is hereditary this statement at once is called into question, for there is no known mechanism in heredity which permits such a peculiar distribution of the disease. If such a distribution occurs between the sexes, it must be accepted, and one must admit that there is no key

to the explanation. It becomes imperative, therefore, that the data be examined to see whether the statement is founded on fact.

A third statement which one encounters is that not only does this disease tend to affect one sex in any given family but it tends to affect all the members of that sex in the family. If the disease is inherited, one is at a loss to explain this statement, for again there is no known mechanism by which such a result could be accomplished.

The present paper attempts to prove the following assertions.

- 1 Xeroderma pigmentosum is inherited, and the term familial is a misnomer not only for this but for any disease and should be dropped.
- 2 Xeroderma pigmentosum is dependent on a set of recessive determiners located in a pair of chromosomes not connected with sex. The method of proof here depends not on experimental matings but on the application of mathematical formulas. It will be shown that the observed data on xeroderma pigmentosum agree with the expectations demanded by the formulas on theoretical grounds. The incidence of cousin marriages among the parents of the patients will be used as further proof of the mode of transmission of this inherited disease.
- 3 The disease tends to affect not more than one child in the majority of families, although the occurrence of two or more affected children in one family is not rare.
- 4 It does not tend to affect one sex only in a family but may affect the two sexes equally.
- 5 Not all the members of one sex tend to be affected in any family, this involvement being the rare rather than the usual occurrence. These misconceptions should disappear from the literature on xeroderma pigmentosum.

IS XERODERMA PIGMENTOSUM INHERITED?

It is necessary first to examine the data on which rests the idea that this disease is not inherited. This belief had its foundation in the old misconception of what is meant by hereditary. Formerly it was thought that for a condition to be called inherited it had to be present in parent and child, generation after generation. When a trait or character suddenly appeared in one or more children of a family, with no previous history of it in the ancestors, it was said to be familial but not hereditary. In practically all cases xeroderma pigmentosum appears in children whose parents and ancestors were not similarly affected. Hence, xeroderma pigmentosum was said to be not hereditary but familial.

Today, of course, this conception has changed, owing to the work of the experimental geneticist, who has shown that in lower forms the so-called familial conditions are just as hereditary as those which descend from generation to generation as obvious characters. They differ from conditions of the latter type, however, in this way. They require a double dose of the determiner before the condition can become obvious.

Two parents both of whom carry but one determiner for the condition and hence do not show the character may produce obviously affected offspring, since each may pass on his or her single determiner to the child. The child thus receives a double quantity, and the character develops as an obvious one. Such characters are said to be due to recessive determiners, in contrast to the characters which are passed on from parent to child, generation after generation, and are said to be due to dominant determiners. But in either case the character is inherited, for it is determined by forces which reside in the germ cells, which are the sole connecting link between parent and child. The term *familial* in contrast to *hereditary* should be dropped from medical literature, as it perpetuates a conception which genetics has shown to be erroneous. Therefore, the fact that the parents of patients with xeroderma pigmentosum are themselves unaffected by the disease in no way militates against the conception that this disease is an inherited one, due to factors which are present in the germ cells. It is merely understood that the disease does not behave as though it were dependent on dominant factors. The fact that it tends to be concentrated in a few families however, leads one to the hypothesis that it may be dependent on recessive determiners.

IS XERODERMA PIGMENTOSUM INHERITED AS A RECESSIVE CHARACTER?

That this disease is inherited and is dependent on recessive factors cannot be proved by the method used by the experimental geneticist—by appropriate matings—but certain mathematical formulas can be applied to the observations which have been deduced from the recognized behavior of conditions proved to be recessive in their mode of inheritance. If these mathematical formulas agree with the observed data, one may conclude that the hypothesis is workable. The more criteria one has by which to test the observed data the stronger will be the proof that the hypothesis is correct, provided, of course, that the data are in agreement with the criteria. To apply these formulas, there must be a large number of cases, and so it is necessary to collect and analyze as many of the reported cases of xeroderma pigmentosum as possible. It is true that the question of the accuracy of diagnosis enters here, but this need not trouble one too much. The characteristics of this disease are rather clearcut, and there is little that is likely to confuse the picture. If there was any question as to the accuracy of the diagnosis the case was omitted from the series reported in this paper.

Although reports of about 460 cases of xeroderma pigmentosum have appeared in the literature, some of these were published in foreign journals which were inaccessible to me. The available accepted cases numbered 170. Since there is no reason to suppose that the cases

TABLE 1—Data on 198 Families in Which Xeroderma Pigmentosum Appeared

A Families with Complete Family History								
Author	No of Children Affected in Family			No of Normal Children in Family			Parents Related	Comment
	Male	Sex		Male	Sex			
		Fe	Not Stated		Fe	Not Stated		
Adrian	1			1			First cousins	Jewish
Anderson	1	1			None			
Andrews		1			None			
*Archambault	2	1		2				
*Bandler	1	2				9		
Becker, Pautrier and Woringer	1			1	5		First cousins	2 children died in infancy
*Bernoulli	2	2				5		
Bowen	1					4		
*Brault		1		1				
Brayton	1	2		3		1	Not related	
Cannon		2	1			3	Not related	Italian
Cunright	1			5	2			five boys and 1 girl died in infancy, paternal grandfather said to have been affected
*Cedercreutz	1	2				4	Not related	Italian
Cedercreutz	1	1				4	Not related	Italian
Cedercreutz	1	1				8	Not related	Italian
Cole and Driver		1		1	1		First cousins	
Copeland and Martin		1		1	2		First cousins	Jewish
Copeland and Martin		3			3		Not related	
Copeland and Martin		1			None		Not related	
Corlett	1				None		First cousins	1 miscarriage at 3 mo
Corson and Knowles	2	1		1	2		First cousins	2 girls died in infancy
Crocker	1	2			1			
*Crocker	1	1			1			
*Danlos	1	1		1	3			
Dennie	2	1		1	1			
*Dörffel		2				6	Related	European stock
Duhring		1		3	1	4		Four children of unknown sex died in infancy
*Eliassow	2	1				5	Not related	
*Engmann	1	1		1				
Fox	2			2			First cousins	
*Freund		2				12	First cousins	
*Fuss		1			1		First cousins	
*Geber		2		1				
*Greeff	2			2	2			
Grindon	1	1		2				Mother freckled heavily
*Hahn and Weil		2			6			
Halle		1				2		
Hayman	1			1			Not related	
Herkheimer	1	1				4		
Hunter	3			1	4			1 child died at age of 2½ years
Hutchins	1				1		First cousins	
*Hyde	1	2		3		2		
Jeanselme and Hufnagel	1					1	Second cousins	
*Junès	1			1	1	1	First cousins	Arab
Junès	1	1				2	First cousins	Arab
Kaposi		2				2		
Kaposi		1		2	6			
Kerl		1				7		
Kessler	1	2		1	2	1	Not related	
*Klein	4			3	2		Second cousins	
Klein			1					Child of 1 of the normal sisters of the preceding family
Kren		1				3		
Kring	1				None			2 half brothers normal
*Kudish	2	1		2	4			
Kudish		2			1	2		
Lane		1			4		Second cousins	
*Lederer	1	1		2				
*Lenz			3			6		
*Lesser and Bruhns		2			1			
*Leszczvinski	2			1	7		Related	

TABLE 1—Data on 198 Families in Which Xeroderma Pigmentosum Appeared
—Continued

A Families with Complete Family History—Continued							
Author	No of Children Affected in Family		No of Normal Children in Family			Parents Related	Comment
	Male	Sex Fe Not maie	Sex Fe- maie	Sex Not maie	Stated		
Lord	1			1		First cousins once removed	
*Lukasiewicz	2			1			
Lukasiewicz	1			2	1		This family and the next family reported by this author were related
Lukasiewicz			1				
Lynch		1				7	Not related
*Mendes da Costa	1	1		1	1		
*Metscheraki	2	1				3	
*Metzenauer	1	1		3	5		
*Migliorini		3		2	1		
Montgomery		1		3	1		Not related
*Monthus		1			None		2 boys died in infancy This child was first cousin of the two in the second family re ported by Monthus
Monthus		2		2			First cousins
Murphy	1	1				5	
*Nemeth	1					2	Second cousins
Nicolas, Favre and Dupasquier	1	1		2	1		
*Nicolas, Favre and Dupasquier		2		2		4	
*Nicolle		1		4	2		Italian
Nicolle	1			2	1		Tunisian
Nicolle	1			1	1		
Nicolle	1				4		French
Nicolle	3			3	1		Tunisian
Nicolic	1	1			1		
*Okamura	1	1			3		
Oulmann	2				None		Parents German and Irish
*Per	1				None		First cousins
Pernet		1			None		Not related
Phillips		1			2		First cousins
Pick	1	2				9	Cited by Taylor
*Piéchaud	2				None		
Potter		1					
Quinquand		2		1			
*Raynaud	2			3	4		These children were half brothers of the affected girl in the second family re ported by Raynaud
Raynaud		1			None		
Rich	2					6	
Rouvlere		3		4	1		Second cousins
Ruder	7			1	5		Cited by Ormsby Cited by Councilman
*Scherber	2			3			Second cousins
Simpson	1	1		9	5		First cousins
Simpson		1					4 normal children died
*Steln		2		2			Several† Second cousins
Steinberg	2				1		The 2 children affected were brothers of the mother of the 2 af fected boys in the second family re ported by Steinberg
Steinberg	2					2	
Stout	1		1			2	
Taylor	1	1		2	2		Second cousins
Taylor		3				7	First cousins
Taylor		1				5	
Taylor		1			None		Jews
*Tenneson	1	1		1	1		Jews
*Teterjanz		3		1	1		These two families re ported by Teterjanz were related

TABLE 1—Data on 198 Families in Which Xeroderma Pigmentosum Appeared
—Continued

A Families with Complete Family History—Continued								
Author	No of Children Affected in Family			No of Normal Children in Family			Parents Related	Comment
	Male	Sex		Male	Sex			
		Fe	Not Stated		Fe	Not Stated		
Teterjanz		2		2				
*Thibierge	1			1			First cousins	These 2 affected children were also first cousins
Thibierge		1		4	2		First cousins	
*Unna			2			4		
Vidal		1		2				Cited by Taylor
Vidal	1			1	1			
Vidal	1			3	1			
*Vidal	3			1	1			
*Vidal		2		2				
Walker		3		None				The half sister by their father's first marriage and the half sister by their mother's second marriage were normal
White	2			2	3			Russian Jews
White		1		Several			Not related	
*White	2			2	2			
Whittle		1		None			First cousins	
Withers	1			1	1			
De Wolf		1				3	Not related	
von Zumbusch	1				2			Several sisters were said to be normal, which I have stated as 2
von Zumbusch		3		1		5	Distant relatives	
B Families with Incomplete Family Histories								
Author	Number of Children Affected in Family			Sex Not Stated	Parents Related		Comments	
	Male	Sex						
		Female	Not Stated					
Adams				1				
Alderson			1		Related			
de Amiels	1		1		Not related			
*Arnozan	3							
*Artom	2							
*Beron			2					
Blackman	1		1					
Chanee	1			1	First cousins		Jewish	
Corlett	1						Father also said to have been affected	
Counsellman and others			2					
*Diaz	1		1		Second cousins			
*Dies	1		1					
Dobell	1						1 sister freckled easily	
Dubois Havernith	1						Cited by Taylor	
Eller	1						Jewish	
Fox	1							
Fuchs			2				Cited by Nelson	
Freeman	1		1					
*Funk			2					
Gotthell	1							
Grier	1		1				The woman in the second family was paternal aunt to the two in the first, the aunt's father and great-grandfather were said to have been affected	
Grier			1					
Guy and Jacob			1		Not related			
Heitzmann	1						Cited by Taylor	
Herxheimer	1		1					
*Jamieson			2					
*Jones	1		1				Tunisian	
Kaposi			1					
Kaposi	1		1				Italian	
Kaposi			1					
Kaposi	1							
Kaposi	1							
*Klewer	2		1					

TABLE 1 —Data on 198 Families in Which *Xeroderma Pigmentosum* Appeared
—Continued

B Families with Incomplete Family Histories—Continued					
Author	Number of Children Affected in Family			Parents Related	Comments
	Male	Female	Sex Not Stated		
*Kreibich	1	1		First cousins	
Kren	2				
Lane	1				
Lane		1			
*Loeb	1	1		Not related	
Louste, Callan and Du courtlaux		1			Jewish
*Low	2				
*Lustgarten	1	1			
Markowitz		1			
*Moberg	3	3			
*Morini	1	1		First cousins	
*Mukai	1			Related	Japanese
Nelsser	2				Cited by Taylor
Nelson			1		
*Nicolle	2		1		Tunisian
*Nobili	1		1		
*Ohmichi	1		2	First cousins	Japanese
*Perls		2			
*Peyri		2			
*Reines		2			
*Rotch		2			
Sachs		1			
Schamberg	2			First cousins	
de Sanctis	2	1			
Seale	1	1			
*Segawa	1	2			Japanese
Simpson	1				
*Stein	2	2			
*Toyama	1		3		Japanese
Toyama		2			Japanese
Vidal		1			Cited by Taylor
Vidal	1				
Vignolo Litati		1		First cousins	
*Volk	1	1			
Way	1				Greek
Williams		1			
von Zumbusch		1			
Total	167	175	19		

* The asterisk indicates the cases which were cited by E. A. Cockayne

† Two of these children were listed as normal in table 2

‡ Three of these children were listed as normal in table 2

reported in the journals to which I had access were different from those the records of which were not reviewed, it is probable that the conclusions drawn from these 170 cases would not be appreciably altered if the entire series of cases were available. Since the analysis of these 170 cases was completed I have had access to the recently published work of Cockayne. In this study he listed many of the case reports which were inaccessible to me and which were collected by Siemens in 1925. He gave full data only on the families in which more than one child was affected, hence, when these cases were included in my analysis without the corresponding data on families in which only one child was affected the results sometimes appeared to be in disagreement with the conclusions derived from the smaller series. This will be taken up in detail later.

If xeroderma pigmentosum is dependent on a pair of recessive determiners located in one pair of chromosomes, one would expect approximately one fourth of the offspring to be affected, as two parents both of whom are hybrids for the condition, and are outwardly normal, will produce children in the proportion of one-fourth normal, one-fourth affected and one-half hybrid like themselves. This proportion may be expressed by the formula $NX \times NX = NN + 2NX + XX$, in which N stands for normality and X, for the presence of xeroderma pigmentosum and N suppresses the appearance of X. But as many families have less than four children and are included in the series

TABLE 2—Data on Families with Xeroderma Pigmentosum in Which Adequate Information Was Given

Number in Family	Number of Families	Total Number of Children	Total Number of Children Affected	Number of Children Expected to Be Affected
1	12	12	12	12.0
2	12	24	15	13.7
3	19	57	29	24.6
4	21	84	36	30.6
5	14	70	26	22.8
6	12	72	28	21.9
7	9	63	19	18.1
8	11	88	23	24.4
9	8	72	21	19.4
10	4	40	9	10.6
12	2	24	6	6.2
13	1	13	7	3.3
14	1	14	2	3.6
16	1	16	2	4.0
Total	127	649	235	215.2

* The average number of affected children in each family was 1.85 ± 0.05 . The average number of children which should have been affected in each family is 1.7. The difference between the two averages is 0.15, which is three times the probable error, 0.05. This discrepancy is due to the fact that this list is weighted by the inclusion of a large number of families in which two or more children were affected and by the exclusion of the families in which but one child was affected. In the original series of 170 cases collected before I added the cases in Cockayne's list, almost perfect agreement was shown between the theoretical and the actual number of children affected, as discussed in the text.

because they have at least one affected child, the proportion of affected to normal children is always higher than the theoretical 1/3. In the 170 case reports which I collected in which adequate data were given the ratio of affected to normal persons was 1/1.9. When Siemens' cases were added the ratio was 1/1.75, both ratios being much too high. One cannot tell how many parents in the community were capable of producing affected offspring but had only normal children, so one cannot include the normal children of these families to bring the proportion of normal subjects up to its correct figure. By the use of appropriate mathematical formulas allowance can be made for this undue number of affected offspring.

In table 2 are arranged the data on all the families on which the requisite amount of information was given, namely, the total number

of children in the family and the number of affected children. For only 127 of the 198 families listed in table 1 did I have adequate data as to the number of normal and affected offspring. In the fourth column of the table is given the number of children actually affected in families of the different sizes, while in the last column of this table is stated the number of children who would be expected to be affected in this number of families of any given size if the disease were dependent on recessive determiners and the parents were normal, as they were in all instances. These percentages are derived by appropriate mathematical formulas. It will be seen that the totals of the columns for the number of children actually found to be affected and the number of children who would be expected to be affected are 235 and 2152, respectively. The average number of affected children in a family is 1.85 ± 0.05 . The average number of children expected to be affected in a family according to the formula is 1.7. The difference between the two averages is 0.15, which is three times the probable error.

But it must be remembered at this point that the cases which were added from Cockayne's list were all instances in which more than one child in a family was affected. He gave no data on 50 cases in which but one child in the family was affected and the total number of normal sibs was 151. In 87 other instances the original record gave no information. The exclusion of these cases makes the total number of affected children and the average number in a family differ greatly from the theoretical expectation. In the original 170 cases which I collected and which were not weighted in favor of any one type, the total number of affected children in families on which adequate data were given was 103, and the total number who would be expected to be affected, according to the theory, was 101.36. The average number of affected children in a family was 1.68 ± 0.09 , and the average according to the theory was 1.66. In this series of cases the difference between the actual and the theoretical figure was 0.02, which is less than one fourth of the probable error, 0.09. The disagreement between the results obtained when the original 170 cases were used and those which were derived after the cases listed by Cockayne were added is due to the fact that the figures for the latter group were unduly weighted in favor of the instances in which more than one child was affected in a family.

This can be seen by referring to table 1. It will be noted from this table that there were 3 two child families in which both children were affected. There were 9 two child families in which but one child was affected. According to expectation, there should have been approximately 18 families of the latter class, or the number of two child families in which one child was affected should have been six times as great

as that of similar families in which both children were affected. There were 8 three child families with but one child affected, when there should have been about 27 families of this type. Similar figures could be given for the rest of the sibships. Thus, there was but 1 six child family with one child affected, when there should have been 15 in proportion to the rest of the six child families. Some of these missing families were those with one child affected on which Cockayne did not give the data, and if they had been included no doubt the results in table 2 would have been in as close agreement as the results for the series of 170 cases, data on which were originally collected.

TABLE 3—Results of Statistical Treatment of Data on 170 Families in Which Xeroderma Pigmentosum Appeared

s	n _s	r _s	s n _s	q ^s	1 - q ^s	$\frac{s n_s}{1 - q^s}$	Corrected Value for p
1	7	7	7	0.750000	0.2500	28.0	25.0
2	8	10	16	0.562500	0.4375	36.5	27.4
3	8	10	24	0.421875	0.5781	41.5	24.1
4	10	17	40	0.316406	0.6836	58.5	29.0
5	6	8	30	0.237304	0.7627	39.3	20.3
6	5	12	30	0.177978	0.8220	36.5	32.8
7	5	11	35	0.133484	0.8665	40.3	27.2
8	6	11	48	0.100113	0.8999	53.3	20.6
9	2	2	18	0.075035	0.9249	19.4	10.3
10	1	3	10	0.050313	0.9497	10.6	23.4
12	1	3	12	0.031676	0.9683	12.4	24.2
13	1	7	13	0.023757	0.9762	13.4	52.2
16	1	2	16	0.010022	0.9899	16.1	12.5

In this table *s* indicates the number of children in the family, *n_s*, the number of families with *s* number of children, *r_s*, the number of affected children in these families, *s n_s*, the number of children, both affected and normal, in these families, and *q^s*, the proportion of normal children expected in a family in which the defect is due to a single recessive gene substitution.

The corrected value for *p*, which should equal 25, or the percentage of children expected to be affected, is derived from the formula $\frac{r_s \times 100}{s n_s}$.

The average of the corrected values for *p* in the last column is 25.7 ± 1.6 . Thus, the probable error of the corrected value for *p* is less than the difference between this value and the theoretically correct value, 25.

This table was based on the data on the 170 cases originally collected, without the addition of the cases cited by Cockayne.

A second method of ascertaining the agreement between the theoretical and the actual figures, if the condition is dependent on recessive factors, is the use of the formula of Hogben. The results of this method are shown in table 3. Here only the original 170 cases were used, for they had not been selected on a familial basis only and so gave a truer picture of the actual ratio of affected and normal children. If all the families which might have had affected children are included, the average percentage of affected children is 25, indicated by *p*. Since some of the families were omitted, owing to the fact that they did not have an affected child, the actual percentage of affected children must be corrected. The corrected value for *p* should be 25 to have perfect agreement between hypothesis and fact. Since the number of families with

one, two or three children is too small for perfect agreement between the theoretical and the actual value for p for each size fraternity, the average value for p for the whole series must be calculated. The average value of p as determined from the last column, table 3, is 25.7 ± 1.6 . The difference between 25 and 25.7 is 0.7, which is less than one half of the probable error, 1.6. Therefore, this method again substantiates the hypothesis that xeroderma pigmentosum is dependent on recessive determiners.

THE SIGNIFICANCE OF COUSIN MARRIAGES

If these statements are correct, namely, that this condition is inherited and that it is dependent on recessive factors and if the sexes are about equally affected, as they are found to be from an analysis of the data in table 1, one would expect to find that the parents of patients with xeroderma pigmentosum are related more frequently than parents in the general population. The matter will be discussed at this point to show that the incidence of consanguineous matings among the parents of affected offspring has a bearing on the question of inheritance of disease.

Let it be supposed that there are two boxes, one on the left, with 99 black cubes and 1 white cube, and a second on the right, containing 50 white and 50 black cubes. The subject takes a white cube from another pile, and being blindfolded so that he chooses at random, he takes a cube from the box on the left. What is the chance that he will hold 2 white cubes in his hand? It is only $1/100$, since there are ninety-nine times as many black as white cubes to be selected. Now the second cube is selected from the box on the right. The chance of holding 2 white cubes in the hand is now $1/2$, since he is just as likely to choose a white as a black cube, the number being equal.

Certain characters may be substituted for the colored cubes. It may be supposed that a black cube represents a person whose skin is normal and who has no factors for xeroderma pigmentosum. A white cube represents a person whose skin is normal but who carries a latent factor for xeroderma pigmentosum. When 2 black cubes or a black and a white cube are held in the hand, they represent matings in which the children can never have this cutaneous disease, but when 2 white cubes are held simultaneously, it represents a mating in which it is possible for the disease to develop in the offspring. The box of cubes on the left represents the general population, in which in my illustration 1 person in every 100 carries a latent factor for xeroderma pigmentosum. The actual number of persons carrying this latent factor is much less than this, and this figure is used merely as a convenient illustration.

The box on the right represents the relatives of the person who carries this latent factor for xeroderma pigmentosum. The much higher proportion of relatives carrying this latent factor is explained by the fact that related persons come from the same germ plasma in part and hence are far more likely to have the same traits than are unrelated persons.

If the person with a latent factor for xeroderma pigmentosum marries a person from the general population (represented by the box on the left) he has 1 chance in 100 of picking a mate with the same trait in latent form. If he mates with a cousin (represented by the box on the right) he has 1 chance in 2 of mating with a person carrying this latent factor. Hence, if he marries a cousin, he is fifty times as likely to have offspring who show xeroderma pigmentosum as though he mates with an unrelated person. Therefore patients with xeroderma pigmentosum are much more likely to come from cousin marriages than from marriages between unrelated persons. If this disease is inherited as a recessive character and a series of instances of the condition is collected, the proportion of cousin marriages should be found to be much higher than that in the general population. Conversely, if a series of cases of any disease is collected which is not known to be inherited and an excess of cousin marriages is found among the parents, one is justified in concluding that the disease is hereditary and that it is transmitted as a recessive condition. An excess of cousin marriages among the parents of patients with such a disease as compared with the percentage of consanguineous matings in the population does not mean, however, that the persons with this disease are more likely to mate with cousins than are other persons who do not have this latent factor.

An illustration will make this point clear. If it were found that parents of patients with xeroderma were related fifty times as often as parents of persons not showing xeroderma, one might be tempted to conclude that some selective factor is at work which induces cousins having the latent trait for xeroderma to marry and to produce affected offspring. The illustration of the boxes of cubes may again be used. To begin with, it is known that about 1 marriage in every 500 in the general population is between cousins, that is 0.2 per cent of matings are consanguineous. Now with the white cube in the hand, representing a person who carries the latent trait for xeroderma the subject makes 10,000 choices from the box on the left, which indicates the general population. Since 1 per cent of the choices are likely to fall on the white cube, there are 100 matings between persons with the latent trait for xeroderma and hence 100 matings which may produce affected offspring. Since a person is five hundred times as likely to choose an unrelated as a related mate 20 choices may be made from the box on

the right for the 10,000 from the box on the left. But of these 20 choices 10 are likely to fall on the white cube, or, in terms of persons, 10 of the 20 matings are likely to be with cousins who have the same trait latent. Therefore these 10 matings result in affected offspring. Thus, of 110 matings in which affected offspring were produced 10, or about 9 per cent, were consanguineous marriages.

As is evident from the experiment, persons with this trait latent do not marry a relative with any greater frequency than persons without this trait, but marriage with a relative having been made, the trait is much more likely to appear. Hence it is found that in a large series of cases cousin marriages are unduly frequent among parents whose offspring show an inherited recessive condition. It has been assumed in this discussion that in this theoretical population xeroderma pigmentosum is inherited as a recessive character, and it is found as a result that cousin marriages occur with great frequency. In actuality one must approach the problem from the other end and find whether there is an excess of cousin marriages and if so, one must reason back to the assumption that the trait in question must be inherited and transmitted as a recessive character.

It must be remembered, however, that the incidence of consanguineous matings is disproportionately high among parents of persons exhibiting inherited recessive traits only when the traits are relatively rare. The more common the trait the nearer the incidence of consanguineous matings approaches that found in the general population, since if the trait is universal one is as likely to find it among unrelated as related persons.

INCIDENCE OF COUSIN MARRIAGES

The observed percentages of children affected with xeroderma pigmentosum in a family having been found to agree closely with the percentages which would be expected if the disease were dependent on a pair of recessive determiners, it may now be ascertained whether there is an undue percentage of consanguineous matings among the parents of the children with this disease, thus furnishing another criterion by which the validity of the hypothesis is tested. Toyama expressed the belief that consanguineous matings play an important rôle in causing this disease. According to Ormsby, he described over 30 cases in Japan and found that cousin marriages were frequent among the parents of the patients in his series.

The 361 cases listed in table 1 occurred in 198 families. There were 26 instances of first cousin marriages, 10 of second cousin marriages and 1 of marriage between first cousins once removed. In 5 instances the parents were related, but the degree of relationship was not mentioned. Thus, the incidence of consanguineous matings was 21.2 per

cent The average incidence of marriages between relatives in the general population varies in different localities, but it has been estimated by Baur, Fischer and Lenz to be about 0.2 per cent In families in which xeroderma pigmentosum appears the parents are related about one hundred and six times as frequently as parents in the general population

If one considers the incidence of cousin matings only when a statement was made as to the relationship between the parents, it is found that in 42 of the 60 instances in which this point was mentioned in the record there was a history of parents who were related, or an incidence of 70 per cent of consanguineous matings This estimate is no doubt too high, for even if the inquiry as to relationship were made, the tendency would be not to include a statement unless the questioner obtained what he considered a positive answer The real incidence of cousin marriages among the parents of patients with xeroderma pigmentosum is probably more than 21 per cent and less than 70 per cent The high percentage of consanguineous matings among the parents of these patients confirms the idea that xeroderma pigmentosum is inherited and that it is dependent on recessive determiners

The conclusion having been reached that this disease is inherited as a recessive character, the following statements must be examined critically, for the laws of inheritance do not support any of these assertions (1) The disease usually affects more than one in a family, (2) only one sex in a family is affected, and (3) all the members of that sex are affected in that family With regard to the first statement, of the 198 families listed in table 1, 82 families had one child affected and 116 had more than one But this table includes all the cases which had been collected by Siemens up to 1925 in which more than one child was affected and none of his cases in which but one child in the family was affected Siemens had collected prior to 1925 146 cases in which one child was affected In my original series of 170 cases 50 instances of this type occurred before 1925 Even if all of these instances were identical with 50 cases in Siemens' list, there were at least 96 such instances prior to 1925 which should be added to the figures just cited Thus the corrected list would show 178 families with one child affected and 116 families with more than one child affected This means that 60 per cent of all families in which xeroderma pigmentosum appeared had only one child affected and 40 per cent more than one This is the same ratio that was found in my series of 170 cases The cases in my series occurred in 108 families, in 65 of which one child only was affected and in 43 more than one child In this series also the incidence of families in which one child was affected was 60 per cent Hence,

it can be stated that, contrary to the statements concerning this disease in the textbooks, the majority of families do not have more than one child affected

This statement sounds paradoxical, for if a disease is inherited would not one expect to find more than one child exhibiting it in any family? One would not if the disease is due to a recessive determiner. Small families are far more common than large, and, it is not until families of six children or more are considered that one expects to find a greater proportion of families having two or more children affected than of families having only one with the disease. Thus, one expects to encounter six times as many two child families in which one child is affected as similar families in which both children show the condition. In the group of three child families 27 families with one child affected will be found to every 10 families with more than one child affected, and so it goes until the group of six child families is reached, in which 1,909 families with more than one child affected are expected for every 1,458 families with but one child who has the disease.

In table 2 it is found that of the 127 families in which the total number of offspring was given, 78 families, or 61 per cent, had less than six children and only 39 per cent more than six. Therefore if the majority of families have five children or less and if more families of that size are likely to have one child affected than to have several, it is obvious that as a rule one child only in the family will be affected. The larger the number of children the more likely is the family to have a second child affected. Despite the fact that families with less than six children are less likely on the whole to have several children than to have one child affected, the possibility that a second child may be affected should always be borne in mind in giving advice to parents concerning the rearing of more children after one has fallen victim to this tragic disease.

Thus, although more small families will have only one child affected than will have more than one, the possibility that more than one child will be affected is by no means remote. On the average, one seventh of two child families in whom this disease appears will have both children affected. One fourth of the three child families in whom this disease appears will have two of the three children affected, and in 1 of every 37 families of this size all three children will be affected. Hence, there is danger in assuring parents that they will not have a second child with the disease.

The statement that one sex only is likely to be affected in a family may now be examined. To examine this assertion critically, one must use only the families in which at least two children were affected and

there was thus a chance for one child of each sex to show the condition. Of the 114 families with more than one child affected both sexes were affected in 52, or 45.6 per cent. In 8 other families in which one sex only was affected but one sex was represented in the family, and hence there was no possibility for both sexes to be affected. In 4 families only boys were affected and in 4 only girls. Thus, in 60 families, or 52.6 per cent, the rule that the disease did not affect both sexes in the family was broken. In 21 other instances in which two sisters or two brothers were affected no statement was made as to whether there were any other children of the opposite sex in the family who may have been affected, and in 8 instances the sex of all the affected children was not given. Apart from these last instances, however, it can be stated that a rule that is followed less than half the time can scarcely be called a rule. The statement that the disease affects one sex only in a family was made on the basis of a few families, and it has been repeated again and again, with no basis in fact. If the disease is caused by a recessive determiner that is not sex linked, it should not be expected to affect one sex only in a family as a rule. I find that the facts support my interpretation as to its inheritance.

The third point will be considered, namely, that not only is one sex alone affected but all the members of one sex in any family tend to be affected. One hundred and ninety-eight families are listed in table 1. From this list must be excluded all one child families, all families in which both sexes were affected and all families in which the affected child was the sole member of that sex in the family. When one considers only the families in which one sex only was affected, those in which at least two of that sex in the family had the disease and those in which the sex of all the unaffected children was given, there are 53 families by which the validity of the rule can be tested.

In these 53 families this rule was followed in 10 instances and broken in 43. A rule that is followed in but 19 per cent of the cases can scarcely be called a rule. It might be claimed that if for all the families with an inadequate family history more data had been given as to the sex and number of normal children in the family, the 10 cases just cited might have been augmented. As the authors who made the statement that all the members of one sex tend to be affected in any given family had no more data on these families than I possess, since they had only the written records on which to rely, it is safe to state that this idea is erroneous and is not borne out by facts. This result is what one would expect, for if xeroderma pigmentosum is inherited as a recessive disease and not as a sex-linked or sex-limited character, there is no known genetic mechanism by which all the members of one sex in one family are affected while the other sex is left untouched.

SUMMARY

1 Contrary to statements made in textbooks of dermatology, xeroderma pigmentosum is found to be inherited, the determiners for which are passed on in the germ plasm from parent to child

2 It is transmitted as a recessive condition, hence parents who are normal themselves may produce affected offspring

3 Consanguineous marriages are found far more frequently among parents of patients with xeroderma pigmentosum than among the general population, the minimal incidence being 21.2 per cent in the series collected

4 The two sexes are affected equally, hence there is no sex linkage

5 There is no tendency for the disease to pick out one sex in any family and to leave the other unscathed

6 Because of the average small size of families, there are more families with one child affected than those with more than one. This does not preclude the possibility or even probability that in any family a second child may be affected

7 There is no support for the statement that the disease, having affected one sex in the family, affects all the children of that sex in the family. It affects males and females equally and may affect both sexes in the same family

8 It is to be hoped that practitioners, when recording the family history in cases of disease which they term familial, will include in their data (1) the number and sex of the affected children, (2) the number and sex of the normal brothers and sisters, (3) a definite statement as to whether or not the parents were related, (4) any history of the disease in former generations and (5) the age at which the normal brothers and sisters died, or were living at the time of recording, so that, if the disease is one which does not begin until several years after birth, all the children who died in infancy or had not yet attained the minimal age of onset can be excluded from the final record. Such data will take little time or space and will make the record valuable not only for clinical purposes but for genetic study

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EXFOLIATIVE DERMATITIS

REPORT OF A CASE WITH AUTOPSY

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Although death from exfoliative dermatitis is not uncommon, there are comparatively few reports of cases in which autopsy has been performed. In 1933 Poole and Wehger¹ found seventeen reports of cases in the literature and contributed four more. To these may be added the case reported by Allison² and that by Nelson,³ making a total of twenty-three cases recorded in which autopsy was performed.

The pathologic changes described in the reports of cases have varied greatly. No particular organ or combination of organs has been uniformly involved. The lungs have been the most frequent site of involvement, presenting the following conditions, named in the order of frequency: bronchopneumonia, desquamation of the bronchial mucosa, edema, hemorrhagic infarcts and multiple abscesses. Fatty degeneration and cloudy swelling have been the most frequent changes noted in the liver. The kidneys have been described as being large and pale, with multiple hemorrhages or tubular desquamation. Submucosal hemorrhages, with or without ulceration, were frequently observed along the gastro-intestinal tract. The changes in the spleen have apparently been of minor importance, simple hyperplasia, which occurred three times, and chronic passive congestion, twice. Aplastic bone marrow and acute diffuse myocarditis were each noted in one instance.

As the pathogenesis of exfoliative dermatitis remains unknown, the recording of isolated cases in which autopsy has been performed seems warranted, in the hope that an accumulation of evidence may lead to an understanding of the underlying pathologic process of the disease. The case described in this paper has added significance in that the patient was recovering from the dermatitis when he suddenly died of coronary sclerosis. It is reasonable to believe that the acute pathologic change

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1 Poole, A K, and Wehger, R T. Fatalities in Exfoliative Dermatitis, *J A M A* 102 745 (March 10) 1933.

2 Allison, J R. Chronic Exfoliative Dermatitis, *South M J* 24 860 (Oct) 1931.

3 Nelson, R L. Acute Diffuse Myocarditis Following Exfoliative Dermatitis, *Am Heart J* 9 813 (Aug) 1934.

observed in postmortem examination is an indication of the pathologic change occurring in the person who recovers uneventfully

REPORT OF CASE

W B R, a white man aged 26, was admitted to the Reading Hospital on Nov 14, 1935. He had enjoyed good health until May 1935, when he observed that drinking milk in any form was followed by nausea, vomiting, fever and occasionally headache. His physician prescribed a "tonic" and advised him to avoid milk and its products and to adhere to a vegetable and fruit diet. Several weeks later he noted the appearance of flat, light tan, slightly raised oval patches on the skin of the abdomen, chest, back and neck.

Despite scrupulous adherence to the diet, he suffered from frequent attacks of nausea and vomiting in the summer months that followed. However, he was able to continue his usual occupation. In the meantime the eruption was gradually disappearing. In September he suffered from pains about the heart and was bed-fast for two days. At that time he began taking three kelpamalt tablets⁴ daily. About October 3 there suddenly appeared a generalized scarlatiniform rash, accompanied by headache and low grade fever but not by nausea, vomiting or sore throat. He was confined to bed. The bright red color gradually faded and was followed by diffuse scaling. The scales were fine at first but later became large, resembling soap chips. Two weeks prior to the patient's admission to the hospital, the skin of the back became moist. The disease process had been moderately pruritic since its inception.

The patient had always been weak. When a child he had suffered from measles, whooping cough, scarlet fever and chickenpox. There was a vague history of the occurrence of rheumatic pain in one knee. He underwent a tonsillectomy at the age of 13. There was no history of a previous cutaneous disorder or of venereal disease, nor had he ever had an intravenous injection.

The patient's father died at the age of 50, of gastric carcinoma. His mother, two brothers and three sisters were living and well. There was no history of tuberculosis or of allergic disease in the family.

The patient was employed in the wood working department of an iron company. In addition, he did considerable professional painting, using oils, water colors and charcoal. He was single and lived with his mother.

Physical Examination—On examination the patient appeared to be asthenic. He seemed comfortable, was cooperative and answered questions intelligently. There was no evidence of cyanosis or jaundice.

The skin of the entire body, except that of the palms and soles, was reddened and covered with laminated papery scales. The scalp and beard were covered with a yellowish crust. The skin of the upper part of the back was moist and oozing, but other portions of the trunk and extremities were dry. The nails were opaque gray, with irregular transverse ridges. The mucous membrane of the eyes, mouth and throat was inflamed. Secondary excoriations with hemorrhagic crusting were present on the extremities, particularly on the buttocks and arms.

The pupils were round, regular and equal and reacted to light and in accommodation. Extra-ocular movements were normal. The conjunctivae and scleras were

⁴ Kelpamalt, which consists of specially dehydrated kelp, malt extract, powdered milk and chocolate, contains the following minerals: calcium, phosphorus, iodine, magnesium, iron, copper, sodium, potassium, manganese, aluminum and sulfur.

of normal color. There was bilateral chronic otitis media with perforation and granulation tissue, especially on the right. Bilateral ethmoiditis was also present, but the tonsils appeared to be normal.

Expansion of the chest was fair and equal on the two sides. The percussion note was resonant throughout, and the breath sounds were normal. The size of the heart was within normal limits. The heart sounds were of fair quality and regular in rhythm. There were no murmurs or thrills. The blood pressure was 116 mm systolic and 76 mm diastolic.

The abdomen was tympanitic throughout. There were no palpable masses or tenderness.

The deep reflexes were normal. All the superficial lymph glands were discretely enlarged.

A diagnosis of generalized exfoliative dermatitis (Wilson-Brocq) was made.

Laboratory Data—The sugar content of the blood was 110 mg and the non-protein nitrogen content 37 mg per hundred cubic centimeters. The Wassermann and Kahn tests of the blood gave negative results. The blood count revealed 4,160,000 red corpuscles, with 79 per cent hemoglobin. The white cells numbered 22,700, with 38 per cent polymorphonuclears, 11 per cent lymphocytes and 51 per cent eosinophils. The urine showed a faint trace of albumin, with from 40 to 50 white cells per high power field.

Course—During his stay in the hospital, the patient's temperature varied from 97 to 99.6 F and his pulse rate from 75 to 135. Treatment consisted in frequent colloid baths, large doses of calcium lactate by mouth, iron and ammonium citrate taken internally and the daily intravenous injection of 250 cc of a 10 per cent solution of dextrose and of 8 units of insulin hypodermically. Under this regimen there was rapid improvement of the dermatitis. The scaling diminished, and the skin became less red. There was less itching, the patient's appetite improved, and he was rapidly regaining strength. Suddenly he died, on the morning of the ninth day in the hospital.

Postmortem Examination—Autopsy was performed by Dr. Erwin D. Funk, two hours after death.

The peritoneum was pale, smooth and glistening and contained no excess of fluid. The intestines were collapsed, except for a small amount of feces. The appendix was normal, measured 18 cm in length and presented no adhesions. It was retrocecal and pointed toward the liver. The cecum was mobile and located in the pelvis. The omentum was thin and filmy, it contained little fat and covered the intestines well.

The left pleural cavity presented some light adhesions anteriorly. The left lung measured 18 by 16 by 5 cm and weighed 210 Gm. It was pale light gray, with few anthracotic markings. It was crepitant throughout. No congestion or edema was present. The right lung measured 20 by 17 by 5 cm and weighed 260 Gm. It resembled its fellow in every respect.

Histologic sections of the lungs showed alveoli normal in size, except in a few areas of partial atelectasis. The alveoli were free from exudate or transudate. The interalveolar capillaries were not engorged. The bronchi were collapsed and free from secretion. The pleural surface presented no abnormalities.

The pericardium was normal and contained a small amount of clear straw-colored fluid. The heart in situ extended 3 cm to the right of the midsternal line in the third interspace and 8 cm to the left of the midsternal line in the fifth interspace. It measured 12 by 9 by 4.5 cm and weighed 240 Gm. On the posterior wall of the left ventricle there was an area of old fibrosis, which sug-

gested that of an old healed infarct. The left coronary artery was closed by a fibrous cord, 1 cm in length, extending distally from a point 1.5 cm beyond the sinus of Valsalva. The right coronary artery presented some ulcerative plaques, which almost occluded the lumen of the descending branch. The left ventricular wall was 1.5 cm thick and the right ventricular wall 0.6 cm. The aortic valve measured 6.5 cm in circumference and contained yellow atheromas in the sinus Valsalva. The leaflets were thin and competent. The pulmonary valve measured 6 cm in circumference and was normal. The mitral valve measured 8.5 cm and showed slight thickening at the base. The tricuspid valve measured 12 cm and was normal. The aorta was marked with numerous atheromas.

Sections of the cardiac muscle of the left ventricle showed approximately one-third replacement by fibrous tissue, which was irregularly distributed throughout the section. In many small areas the remaining muscle cells had become cloudy, stained poorly and had indistinct nuclei. The fibrosis extended into the papillary muscles. The epicardial and endocardial surfaces were clear. Sections of the left coronary artery showed an atheromatous process, involving the entire media and encroaching on the lumen, so that it was reduced to less than one-fifth of its normal extent. The lumen was eccentric but lined with normal endothelium. The involved portion of the media showed many areas of cholesterol crystals and additional areas of calcium deposition. The lumen contained no thrombus. Sections of the aorta showed an active atheromatous process and no specific destruction of elastic fiber elements.

The liver measured 30 by 19 by 7.5 cm and weighed 1,490 Gm. The surface was pale bluish, smooth and glistening. The cut surface had a pale yellowish tinge on a reddish-brown background.

Sections of the liver showed undisturbed lobular architecture. The hepatic cells were swollen, their cytoplasm granular and their cell membranes indistinct. Throughout the lobule the cells contained many fat globules in the cytoplasm. The blood sinusoids were not engorged. The Kupffer cells were well preserved.

The spleen measured 14 by 10 by 5 cm and weighed 340 Gm. The surface was smooth, wrinkled and dark purple. The cut surface showed a soft pulp with increased fibrosis.

Sections of the spleen showed somewhat enlarged malpighian bodies, but there was no hyperplasia of the reticulum cells. The pulp was greatly congested, all the blood sinusoids were engorged. Eosinophils were particularly noticeable in these sections. An increase in the fibrous tissue and pigment of the organ was not present.

The left kidney measured 12 by 5.5 by 4 cm and weighed 190 Gm. The capsule was smooth and pale and stripped with ease. The exposed cortical surface was pale grayish red. The cut surface was pale grayish and bulged from beneath the capsule. The ureter was single and patulous. The right kidney measured 12 by 6 by 3.5 cm and weighed 170 Gm. It resembled its fellow in every respect.

Sections of the kidney showed a diffuse dense infiltration of the stroma by lymphocytes. These cells seemed equally distributed in the cortex and medulla, and the arrangement did not suggest a specific etiology. Within the cortex were a few scars containing fibrosed glomeruli. An old organized complete thrombus occupied one of the larger arterial branches. The remaining glomeruli showed no change. The tubule cells were swollen, and many had undergone hydropic degeneration.

The prostate gland, gallbladder, stomach, small intestine and pancreas were found to be normal, on both gross and histologic examination.

The large intestine was normal, except for the presence of a dark red polyp, the size of a cherry stone, in the cecum. Histologically the growth was composed of glandular structures, resembling normal intestinal glands, supported by congested and edematous stroma and infiltrated by leukocytes of all kinds. All the surrounding intestine was normal.

SUMMARY

A case of exfoliative dermatitis of undetermined etiology with observations made at autopsy is recorded. The dermatitis was responding favorably to treatment when the patient died suddenly of coronary sclerosis.

The chief observations at autopsy were as follows: healed infarction of the myocardium with atheromata of the left coronary artery, causing almost complete obstruction, atheromatous plaques of the aorta, cloudy swelling, passive congestion and early fatty degeneration of the liver, arterionephrosclerosis, cloudy swelling and chronic pyonephritis of the kidneys, and passive congestion and mild hyperplasia of the spleen.

238 North Fifth Street

Clinical Notes

FILTERED ULTRAVIOLET RAYS

An Inexpensive Unit for Their Isolation

GEORGE M. LEWIS, M.D., AND MARY E. HOPPER, M.S., NEW YORK

The phenomenon of fluorescence noted in many substances when they are observed under filtered ultraviolet rays is of great value to the dermatologist. Margarot and Devèze¹ first drew attention to the value of the rays as a diagnostic measure in infections of the scalp with *Microsporon*. Other observers² have confirmed their observations.

The use of the rays has been extended to many different medical and other scientific fields. In dermatologic practice the important fluorescent effects noted when the filtered ultraviolet rays are used as a sole source of light may help to detect pathologic conditions and to differentiate fungi in cultures.

1 In cases of tinea capitis the value of the rays cannot be overstressed, not only in establishing a diagnosis but as an aid in following the progress of the disease and of determining when cure has taken place. Furthermore, in certain infections with *Microsporon Audouinii* when regrowth of hair is considerable the diagnosis of tinea capitis may not be suspected. In such instances, when only scaling of the scalp may be noted, fluorescence of the affected hairs is characteristic. Patients with this condition before the disease is recognized constitute a serious menace, as they are potential foci for dissemination to other children.

(a) In all types of infections due to *Microsporon* the affected hairs appear as luminous short yellowish green "stubs."

(b) In infections with *Trichophyton endothrix* the affected hairs are dull and bluish. This observation³ is not in agreement with that of Davidson and Gregory,⁴ who stated that hairs infected with *Achorion Schoenleini* fluoresce like those infected with *Microsporon* and that all the hairs infected with *Trichophyton* do not fluoresce. It is true that hairs present in follicles invaded by *Trichophyton*

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University, George M. MacKee, M.D., Director.

1 Margarot, J., and Deveze, P. Aspect de quelques dermatoses en lumière ultraparaviolette—note préliminaire, *Bull. Soc. d. sc. méd. et biol. de Montpellier* 6:375 (June) 1925.

2 Goodman, H. Fluorescence, Particularly in Dermatology, *Brit. J. Dermat.* 40:105 (March) 1928. Cleveland, D. E. H. "Wood Light" in *Dermatologic Diagnosis with Special Reference to Ringworm*, *Arch. Dermat. & Syph.* 18:368 (Sept.) 1928.

3 Lewis, G. M. Ringworm of the Scalp. Curability, Without Depilating Measures, of Infections Caused by "Animal" Microsporons, *Am. J. M. Sc.* 189:364 (March) 1935.

4 Davidson, A. M., and Gregory, P. H. Note on an Investigation into the Fluorescence of Hairs Infected with Certain Fungi, *Canad. J. Research* 7:378, 1932.

ectothrix do not fluoresce, but in our experience in every case of infection with *Trichophyton violaceum* (endothrix) fluorescence of the infected hairs was a useful observation

(c) In infections with *A. Schoenleini* the color is greenish but less luminous than in the infections with *Microsporon*

2 Animal carriers (particularly kittens) of certain pathogenic fungi may be detected⁵ by fluorescence of affected hairs which when observed under filtered ultraviolet rays have an appearance identical with that of human hairs affected with the disease

3 Various fungous growths in culture may be distinguished⁶ by their characteristic fluorescent colorations

4 *Tinea versicolor* and *erythrasma* show individualistic colors sufficient not only to establish the correct diagnosis but to determine the extent of the eruption even when it has faded so that its presence cannot be clinically detected⁷ Other fungous eruptions, such as *tinea circinata*, *tinea cruris*, *dermatophytosis* of the feet and the secondary eczematous and dyshidrotic eruptions of the hands and other parts, infections with *Monilia* as well as the deep fungous infections (*sporotrichosis*, *actinomycosis*, *blastomycosis*, *coccidioidal granuloma*, etc.) do not fluoresce in any characteristic fashion when observed under filtered ultraviolet rays

5 Hairs affected by *leptothrix* fluoresce

6 Keratin fluoresces, and when it is increased more luminosity may be seen The palm is brighter than the dorsum of the hand Normal teeth and nails fluoresce brilliantly The differentiation of certain diseases of the nails is being investigated by us at the present time Warts and keratoses show a bright fluorescence, while molluscum bodies exhibit a dark center

7 Some fading and indistinct eruptions become clearer when observed under filtered ultraviolet rays⁸ An accentuation of the syphilitic roseola is frequently apparent, and this finding is useful when the diagnosis is not easily made, particularly when concomitant findings are absent Lentiginous and pigmented lesions usually appear darker when seen under filtered ultraviolet rays than when observed in ordinary light

8 Many inorganic substances fluoresce When a drug such as salicylic acid or a product such as petrolatum is present on skin examined under filtered ultraviolet rays the underlying condition may be masked

Since filtered ultraviolet rays are of such importance, a suitable unit for their isolation not only appears to be a necessary part of every dermatologist's equipment but should also prove a useful aid to the general practitioner The following discussion covers the more essential details and offers suggestions for the construction of an inexpensive unit for attachment to an ultraviolet lamp

5 Davidson, A. M., and Gregory, P. H. Kitten Carriers of *Microsporon Felineum* and Their Detection by the Fluorescence Test, *Canad. M. A. J.* **29** 242 1933

6 Lewis, G. M. Fluorescence of Fungus Colonies with Filtered Ultraviolet Radiation (Wood's Filter), *Arch. Dermat. & Syph.* **31** 329 (March) 1935

7 Lewis, G. M., and Hopper, M. E. Pseudo-Achromia of *Tinea Versicolor*, *Arch. Dermat. & Syph.*, to be published

8 Meyer, J., and Saldman, L. Application of Wood's Light to Dermatologic Diagnosis, *Bull. Soc. franç. de dermat. et syph.* **32** 369, 1925

SOURCE OF ULTRAVIOLET RAYS

As a rule, it is not practical to use the sun's rays as a source of ultraviolet rays. However, any of the ordinary office lamps for the production of ultraviolet rays, whether air cooled or water cooled, is suitable for this purpose. Less expensive lamps are also serviceable although the heat generated is a drawback. Davidson and his co-workers⁹ have devised two different lamps which are portable and have proved satisfactory for the detection of tinea capitis. The directions given for their construction, however, are rather vague in certain particulars. Another source of light is a commercial lamp used for indoor photography in which there is an overloaded filament to produce the requisite bright light, with a correspondingly shorter life than with ordinary lamps. Although the content of optimum rays from its beam is not so great as that of the beam of the aforementioned lamps, it is nevertheless a satisfactory substitute for an ultraviolet lamp. It may also be used to differentiate fungous growths in culture.

FILTER

The type and thickness of the glass filter through which the ultraviolet rays pass are of great importance. This is especially true in observations on the fluorescent colorations of cultures of fungi. Divergent results may be obtained by different observers owing to a difference in the type of glass filter or in its thickness. We have found that the wave lengths in the near portion of the ultraviolet part of the spectrum (in the region of 3,650 angstrom units) offer optimum fluorescent value. Many different types of glass have been tried, the Corning glass violet ultra,¹⁰ no. 586, polished to a thickness of between 4 and 5 mm is adequate for use. In its molded form it is usually from 7 to 8 mm in thickness, and unless the source of light is extremely powerful, not enough ultraviolet rays are transmitted to produce the desired results. This filter is a sodium barium silicate glass and contains slightly less than 9 per cent nickel oxide. As the glass is not heat resistant care must be exercised that overheating does not take place, or cracking will result.

EXCLUSION OF UNWANTED RAYS

The room in which the examination is made must be darkened, and in addition most of the visible rays from the ultraviolet lamp must be excluded by a suitable attachment so that only rays of light from the lamp which are not absorbed will pass through the filter. A tinsmith's services may be utilized, or a molded copper attachment may be fitted to the lamp, leaving an open slot for the filter.¹¹ The disadvantages of such a device are (1) that the attachment is not transferable to a different make of lamp or, often, to a different model of the same make of lamp and (2) that the equipment may be cumbersome, heavy and difficult to store or transport. When the source of light generates considerable heat suitable provision must be made for ventilation.

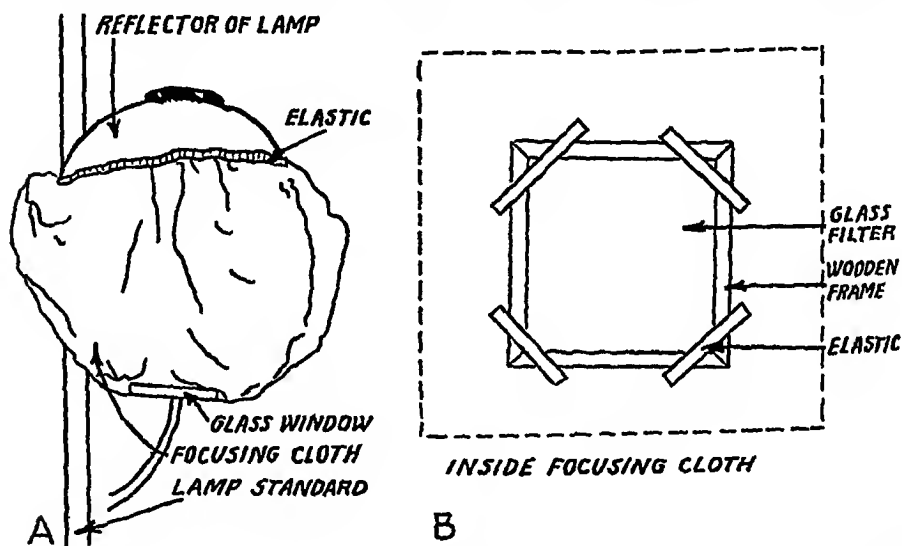
9 Davidson, A. M., and Gregory, P. H. A Convenient Source of Wood's Light for the Diagnosis of Ringworm of the Scalp, *Canad. M. A. J.* **27**:176, 1932. Davidson, A. M., Boyd, S. A., and Haltain, C. P. An Improved Source of Ultraviolet Light for the Diagnosis of Ringworm of the Scalp, *Canad. M. A. J.* **33**:534 (Nov.) 1935.

10 The Corning Glass Works, Corning, N. Y., furnishes violet ultra, no. 586, 6½ inches (16.51 cm.) square, polished on one side to a thickness of 4.5 mm., for \$4.75, carrying charges are extra.

11 Mr. Harry Ashmore, an engineer, made a satisfactory attachment of this type for us.

OUR METHOD

The unit herewith described is light, easily attached and detached and readily stored, and it has proved durable in our hands. Any of the better makes of lamp for the production of ultraviolet rays may be used as a source of light. The material needed for the construction of the attachment is 1 square yard of light-proof black rubberized focusing cloth (obtainable at a camera shop). A hole 5 inches (12.5 cm) square or smaller¹² is cut near the center of the cloth. The edges of the hole are hemmed. Then the glass filter is placed over this hole, overlapping the cloth on each side. Elastic loops are sewed diagonally across the four corners to hold the glass in place. If the fit is snug no light will seep around the edge of the glass. A hem is sewed around the edge of the cloth, in which is placed an elastic draw string. The cloth is then held up to and placed around the hood of an ultraviolet lamp, and the elastic draw string is tightened until the fit is close enough to exclude visible rays (fig A). The ends of the draw string may then be sewed together so that later the cloth may be quickly



A, authors' device attached to an office lamp for the production of ultraviolet rays, B, inner aspect of the device, showing method of attachment of glass filter to the focusing cloth

stretched around the hood of the lamp. In order to protect the glass filter from breakage a wooden frame may be glued to its edges (fig B). When lamps that produce considerable heat are used the cloth may not wear well because of its rubber content. This objection does not arise when a better make of lamp is used. The approximate cost of the attachment (with $6\frac{1}{2}$ inch [16.51 cm] square filter) is \$5.50.

SUMMARY

The important uses of filtered ultraviolet rays in dermatologic practice are enumerated.

An inexpensive, easily constructed unit for the isolation of rays of the correct wave lengths with which satisfactory fluorescence may be obtained is herewith described.

200 West Fifty-Ninth Street

¹² The size of the hole depends on the size of the glass filter. It is suggested that a hole 5 inches (12.5 cm) square be used when the glass filter is $6\frac{1}{2}$ inches (16.5 cm) square.

Minor Notes

GLYCERIN AND BENZOIN LOTION

H N COLE, M D, AND TORALD SOLLMANN, M D, CLEVELAND

There is a real need for an inexpensive, practical hand lotion. A lotion, to be satisfactory, should make the skin soft, should not be too drying and should be easily applied. It is even better if, in addition to possessing these qualities, the lotion can be easily prepared.

Benzoin has been used a great deal in preparing hand lotions. One method of preparation has consisted in putting a few drops of tincture of benzoin in glycerin and rose water. However, the resin of the benzoin, which is insoluble in the mixture, had a tendency to separate as a milky emulsion or to form a sticky mass.

Another method has consisted in inserting a bag of gauze containing benzoin into heated glycerin and then adding the rose water. In this way a little of the benzoin was absorbed, but that method too has been unsuccessful.

A greatly superior hand lotion, which we have employed for years and which we have found to answer all the requirements is obtained by the use of a formula furnished by one of us (Dr Sollmann). The method of preparation consists essentially in macerating benzoin (Siam benzoin) (3 per cent) in a mixture of glycerin and alcohol (3:1 by volume). The addition of the alcohol is the important feature of the process, it secures a better solution of the benzoin, and it "cuts" the viscosity of the glycerin, so that it spreads easily on the skin, leaving a thin layer when the alcohol has evaporated. The working formula is as follows:

Glycerin	640 cc
Alcohol	240 cc
Perfume (white lilac)	10 cc
Water	80 cc
Mix thoroughly and add Siam benzoin	30 Gm

Siam benzoin makes a better lotion than the ordinary benzoin used commercially. The preparation is allowed to age for at least a week, but best results will be achieved if it is allowed to stand for from four to six months, thereafter the preparation may be decanted as necessary for use. It makes a perfectly clear, light yellowish liquid, pleasantly though not too strongly perfumed. The lotion is employed after washing and drying the hands. It is necessary to warn the user to employ only 2 or 3 drops. If a large amount is used the lotion is sticky, on the other hand, if only a small amount is employed, the skin is kept delightfully soft and free from cracking and scaling. The lotion is of practical use for physicians, dentists, housewives and other persons who must frequently wash the hands.

1352 Hanna Building

PRESERVATION OF FUNGUS COLONIES BY FORMALDEHYDE

GEORGE M LEWIS, M D, AND MARY E HOPPER, M S, NEW YORK

An unwanted alteration in the appearance of many pathogenic fungi in culture referred to as pleomorphism¹ or monomorphism² may be retarded by keeping the fungus colony in a refrigerator or by transferring it to a growth-retarding medium. It may be impossible, however, to prevent the transition from occurring eventually. When the change occurs, a colony loses its typical appearance and may not be identifiable by its gross characteristics. Furthermore, it may be impossible in subsequent transfers to recapture the appearance of the original growth, and its identity may be permanently lost. Colonies of rare species of fungi, particularly, may not be in the best condition when they are needed for teaching purposes. By the method here described a fungus colony may be preserved in its typical form for an indefinite period. The gross appearance of the colony will remain unchanged for many months. The appearance under filtered ultraviolet rays,³ however, changes to a noncharacteristic, dull color as soon as the growth is killed. A further advantage is that in keeping a virulent pathogen, such as *Coccidioides immitis*, for display purposes all danger of accidental human inoculation is eliminated.

METHOD

When a fungus colony has acquired a characteristic appearance, the cotton pledget is moistened by being dipped in a 40 per cent solution of formaldehyde and then replaced in the test tube. The growth is killed within twenty-four hours. The opening in the test tube should then be stoppered with a cork, or the cotton pledget may be dipped in paraffin so as to make a completely air-tight seal. This precaution is necessary to prevent evaporation of moisture from the agar with a resultant shriveling of the fungus growth.

SUMMARY

It is possible by the method here described to collect a permanent instructive exhibit of pathogenic fungi in culture.

200 West Fifty-Ninth Street

From the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University, George M MacKee, M D, Director

1 Sabouraud, R. *Les teignes*, Paris, Masson & Cie, 1910

2 Fox, H. *Some Fungous Infections of the Skin and Appendages*, Atlantic M J **30** 273 (Feb) 1927

3 Lewis, G M. *Fluorescence of Fungus Colonies with Filtered Ultraviolet Radiation (Wood's Filter)*, Arch Dermat & Syph **31** 329 (March) 1935

HERPES ZOSTER WITH PARALYSIS OF ONE SIDE OF THE FACE

ARTHUR G SCHOCH, M D, DALLAS, TEXAS

Because paralysis of one side of the face is an infrequent complication of herpes zoster involving the superficial cervical plexus and because of the prompt favorable response to treatment with solution of posterior pituitary U S P this report is made

REPORT OF A CASE

H L P, a man aged 26, single, was seen on July 19, 1935, with lesions of herpes zoster involving the right side of the neck below the mandible, the lobe of the right ear and the right mastoid region. The duration of the eruption was five days. There were several enlarged, tender lymph nodes behind the angle of the right mandible. Seven groups of herpetic lesions were present.

There was complete paralysis of the right side of the face which had been present for only one day.

The patient was given 1 cc of solution of posterior pituitary U S P hypodermatically on the first, second and fourth days.

Symptomatic improvement was noted after the second injection, and ten days after the last treatment both the herpetic lesions and the paralysis of the right side of the face had completely disappeared.

COMMENT

The peripheral nerves involved were apparently the great auricular nerve and the cervical nerves in the skin. These nerves originate from the cervical plexus (second, third and fourth cervical nerve roots). A branch of the great auricular nerves communicates with the seventh nerve after that nerve leaves the stylo-mastoid foramen before dividing to supply the muscles of the face. A lesion at this site, an infectious neuritis, would explain the clinical picture in this case. An infection limited to the nuclei of the posterior nerve roots of the second and third cervical nerves would not explain the facial paralysis.

Furthermore, the facial paralysis was complete and hence peripheral, it was probably due to edema without destruction of the nerve fiber, otherwise complete recovery from facial paralysis in fourteen days could not have occurred.

1717 Pacific Avenue

News and Comment

PROGRAM NOTICE, ATLANTIC CITY MEETING OF AMERICAN MEDICAL ASSOCIATION

Applicants for a place on the program of the Section on Dermatology and Syphilology of the American Medical Association at the meeting in Atlantic City, N J, from June 7 to 11, 1937, are requested to submit titles and provisional abstracts of their proposed papers to the secretary of the section, Dr Bedford Shelmire, Medical Arts Building, Dallas, Texas

Applicants need not be members of this section but must be Fellows of the Association, graduates in medicine not in private practice or invited guests

PERSONAL

In the July issue of the ARCHIVES it was announced that Dr Mihran B Parounagian had resigned his position as visiting dermatologist and syphilologist to Bellevue Hospital on account of ill health. Fortunately, Dr Parounagian has recovered and is again active in private practice

Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

ROENTGEN-POSITIVE SERONEGATIVE INFANTILE CONGENITAL SYPHILIS NORMAN R INGRAHAM JR, *Am J Dis Child* 50.1444 (Dec) 1935

Ingraham states that in the year from Jan 1 to Dec 31, 1934, at the Philadelphia General Hospital, though the incidence of syphilis among the pregnant women was 11.8 per cent and the majority of the patients received insufficient prenatal antisyphilitic therapy to insure the birth of healthy children, not one of the 1,517 babies discharged alive from the maternity division showed any clinical evidence of congenital syphilis. The Wassermann reaction was of value in diagnosing syphilis in not more than 9 syphilitic children among 195 offspring of syphilitic mothers. The roentgenogram discovered 40 additional cases, 26 (19.4 per cent) being recognized before the patient was 6 days old and 23 cases (17.1 per cent), when the patient was from 1 to 10 months old. In all these cases the initial skeletal changes were evident roentgenographically before the blood serum gave a positive reaction.

Treatment of the mother before delivery affects the early roentgenographic evidence as follows. Of 51 cases in which the mothers were treated more than two months, in 5 (9.8 per cent) syphilis was shown in the infants roentgenographically at 6 days, of 68 cases in which the mothers were treated less than two months, in 21 (30.8 per cent) there was positive roentgenographic evidence of syphilis in the offspring. Cases in which the roentgenograms revealed no positive signs at the age of 6 days were studied at ages from 3 to 6 months. Of 36 cases adequately followed, in 12 (33 per cent) the roentgenographic evidence subsequently became positive.

In 3 cases serial roentgenograms of the same child taken over a period of several months are shown, leaving no reasonable doubt that the earlier changes in the bones seen a few days after birth are the precursors of the more advanced and easily recognized osseous lesions which developed subsequently. The Wassermann reaction which originally was negative became positive as the disease progressed, making a syphilitic etiology seem certain. **AUTHOR'S SUMMARY**

KAPOSI'S VARICELLIFORM ERUPTION EDWARD F CORSON and JOHN B LUDY, *Am J Dis Child* 50.1476 (Dec) 1935

Corson and Ludy report three cases of Kaposi's varicelliform eruption, two occurring in infants and one in a boy 9 years of age. The three patients had suffered from a previous eczema. The eruption resembled variola a great deal more than varicella. The lesions were umbilicated pustules of quite uniform size. Constitutional symptoms associated with fever and malaise were present. Healing occurred without scarring. The authors state that previous vaccination for smallpox and bullous erythema multiforme must be considered in the differential diagnosis. The areas involved are the face, neck, hands, wrists and forearms.

SUCCESSFUL TREATMENT OF NOMA WITH FORMALDEHYDE S I McMILLEN, *Am J Dis Child* 50.1495 (Dec) 1935

McMillen reports two cases of noma (gangrenous stomatitis). In one case treatment with fuming nitric acid was of no avail. In the other case after fuming nitric acid had failed to stop the spread of the disease, undiluted formaldehyde (British Pharmacopoeia) was applied once daily for five days, and an exceedingly satisfactory result followed.

THE INFLUENCE OF INADEQUATE TREATMENT OF EARLY SYPHILIS ON THE INCIDENCE AND INCUBATION PERIOD OF NEUROSYPHILIS J E KEMP and W C MENNINGER, Bull Johns Hopkins Hosp 58 24 (Jan) 1936

This study was made to test the validity of the assumption that inadequate treatment of early syphilis not only increases the incidence of neurosyphilis but shortens the interval between infection and the appearance of clinical evidence of neurologic damage. In a study of 680 patients, 265 of whom had neurosyphilis, Kemp and Menninger made the following observations: 1. Inadequate treatment given early (within two years after infection) apparently does not increase the incidence of neurosyphilis. When no treatment was given the percentage of cases of neurosyphilis was 52.6, and when inadequate treatment was given early it was 43.4.

2. The incidence of neurosyphilis in male patients given no treatment and in those given inadequate treatment was 57.4 and 57 per cent, respectively. In female patients the incidence in the group given inadequate treatment was 32.2 per cent, and in the group given no treatment, 50 per cent. Thus, by comparison of the incidence in a group without treatment, it appears that in females inadequate treatment given early reduces the incidence of neurosyphilis.

3. The incubation period of clinical neurosyphilis was reduced approximately five years in a group of patients who received inadequate treatment early in the disease as compared with a group receiving no treatment, i. e., it was reduced from nineteen and two-tenths to thirteen and one-tenth years in males and from fourteen and nine-tenths to eight and seven-tenths years in females.

4. The incubation period of neurosyphilis was shorter in females than in males both in the treated and in the untreated group. The reason for this difference is not apparent from this study.

NELSON PAUL ANDERSON, Los Angeles

SENSITIVITY TO INGESTED YEAST J B BIEDERMAN, J A M A 106 31 (Jan 4) 1936

Ingested yeast was found by Biederman to be responsible for allergic diseases in four patients. The response to the allergin differed in each patient, producing asthma in the first patient, eczema in the second, hay fever in the third and urticaria and angioneurotic edema in the fourth. Confirmation in each case was established by positive cutaneous reactions to tests with yeast and by the return of symptoms after ingestion of yeast when its withdrawal from the diet had resulted in a disappearance of the allergic response. Biederman suggests that tests with yeast be included in routine cutaneous tests.

RECOMMENDATIONS FOR A VENEREAL DISEASE CONTROL PROGRAM IN STATE AND LOCAL HEALTH DEPARTMENTS SUMMARY REPORT OF AN ADVISORY COMMITTEE TO THE U S PUBLIC HEALTH SERVICE R A VONDERLEHR and others, J A M A 106 115 (Jan 11) 1936

In a report by an advisory committee to the United States Public Health Service, a broad and comprehensive program to control venereal disease was outlined. The following points were emphasized: The organization of the program should be in the hands of a full time officer, who should have a local advisory committee. Adequate funds should be available to provide requisite facilities for treatment of indigent patients and to take care of emergencies. In rural districts, subsidies to counties and communities might be required to transport patients to the nearest center of treatment. In each state at least one or two centers for diagnosis and treatment of venereal diseases should be established in which, among the other services, roentgen and other special laboratory facilities should be provided. Such centers should be consultant in nature. To prevent hereditary syphilis, a blood test should be made of every pregnant woman, and when the test is positive, antisyphilitic treatment should be given. Follow-up or epidemiologic investigation of each infectious case and also of cases in which lapse from treat-

ment has occurred is considered essential. Adequate laboratory facilities should exist, emphasis should be laid on dark-field examinations and lumbar punctures. The health departments should cooperate with private physicians by providing free diagnostic service and free antisyphilitic drugs when the patient is a menace to public health and by making consultation services available. The collection of adequate morbidity and mortality reports should constitute an important function of the officer in charge. Informative literature should be disseminated among physicians, nurses and other workers. Undergraduate and postgraduate training should stress the efficient handling of venereal diseases. Educational material should be disseminated among the general public.

TORULOSIS LOUIS A MITCHELL, J A M A 106 450 (Feb 8) 1936

The patient whose case is reported contracted the disease two weeks before he was first observed. He complained of frontal headache, weakness and dizziness. He was also nauseated and vomited frequently. His mental state was stuporous, and he was quite restless, excitable and apprehensive. There were marked photophobia and nystagmus, the muscles of the neck were spastic, and the patellar reflexes were absent. The hemoglobin content was 50 per cent, the total leukocytes numbered 7,000, and there were 95 per cent polymorphonuclears. The spinal fluid was cloudy and was under high tension. Mycologic examinations revealed heavy walled, round bodies with buds. Gram stain showed gram-positive budding yeast-like bodies. An india ink preparation revealed a wide capsule. The average diameter of the organism was 21 microns. The organism was grown on several different mediums. Fermentation tests gave negative results. Mitchell also comments on the literature, pointing out that various internal organs and the skin may be infected with this organism. The infection is of low pathogenicity until the central nervous system is invaded, at which time the clinical course becomes fairly rapidly fatal. The association of torulosis and Hodgkin's disease appears to be more frequent than could be accounted for by the theory of probability.

COOPERATIVE CLINICAL STUDIES IN THE TREATMENT OF SYPHILIS SYPHILIS IN PREGNANCY HAROLD N COLE and others, J A M A 106 464 (Feb 8) 1936

It was shown that even inadequate antisyphilitic treatment administered during pregnancy is of value to the unborn child. The desideratum is continuous treatment during the entire period of each pregnancy for any syphilitic patient, and it is particularly desirable that treatment be administered before the fifth month of the pregnancy. In cases in which early stages of syphilis developed late in the pregnancy, treatment until the termination of the pregnancy proved to be of value. In only 7.6 per cent of the cases in which treatment for early stages of syphilis was given after the fifth month of the pregnancy were the children born dead, whereas in control cases in which no treatment was administered the incidence of stillbirths was 46 per cent. Pregnant syphilitic women were found to tolerate antisyphilitic treatment as well as, or better than, syphilitic women who had not been pregnant since they contracted the infection.

LEWIS, New York

ORAL DESENSITIZATION TO COMMON FOODS BEATRICE M KESTON, IRENE WATERS and J GARDNER HOPKINS, J Allergy 6:431 (July) 1935

The method of making dilutions of the more common foods is given. The first dilution is calculated to make the initial dose contain 1 mg of protein. The dose is increased every four days. If symptoms recur the dose is decreased to that of twelve or sixteen days previous. If the symptoms continue the desensitization is discontinued until they subside.

The method has been used successively for five years in desensitizing persons sensitive to the common foods, especially children with chronic allergic eczema.

Any one interested in this subject should send to the authors for a reprint. It is said to contain lists of foods to be avoided during desensitization. These lists are omitted from the article because of their length.

HOYER, Cincinnati [AM J DIS CHILD]

THE EFFECT OF THE ANGLE OF INCIDENCE UPON THE DOSE OF X-RAYS ABSORBED BY THE SKIN. E. H. MOLESWORTH and A. R. RIDDLE, *Brit J Dermat* 47 152 (April) 1935

Molesworth and Riddle show that the angle of incidence of a beam of roentgen rays has little or no influence on the dose actually absorbed in tissues immediately below the surface irradiated. They arrived at this conclusion by mathematical calculations and by the use of a photographic film. Two strips of a photographic film were used. One strip was put in a plane normal to the beam of roentgen rays, and the other was tilted at an angle of 45 degrees. The strips were exposed under uniform conditions and developed in the same tank at the same time. The amount of clouding noted in both strips was the same. Therefore it was proved that the amount of roentgen rays absorbed is not dependent on the angle of incidence but on the energy applied (intensity).

In applying this knowledge to irradiation of the scalp in cases of tinea tonsurans, the authors found that when the five point irradiation according to the method of Adamson and Kienbock was used the areas between the centers of irradiation received an amount of roentgen irradiation far in excess of that applied at the centers. The increased dose in the areas of overlap is dependent on the focal skin distance. Calculations based on the law that the intensity varies inversely as the square of the distance show that the use of any focal skin distance greater than 85 cm causes an overdose in the region of overlap. This distance is impractical because it brings the head too close to the tube and because only the middle third of two adjacent centers receives overlapping irradiation. Complete overlapping is necessary to achieve even distribution of dose, and in order to obtain this the focal skin distance must be increased.

Molesworth and Riddle make the following statement:

"If a system of irradiating can be evolved so that the disparity of dose distribution is considerably reduced, the margin of safety should be wide enough to permit the performance of x-ray epilation with almost complete safety in all cases."

[I have suspected for several years that an overdose of roentgen rays was applied to the areas between centers of irradiation in the five point technic of Adamson and Kienbock for epilating the scalp. I never carried out experiments to prove or disprove this theory. The mathematical and physical calculations of Molesworth and Riddle conclusively show that an overdose occurs in the areas of overlap and that the amount of irradiation absorbed by a few millimeters of tissue is independent of the angle of incidence. The point mentioned by the authors and the fact which should be emphasized is that the margin between the smallest dose that will cause epilation and the largest dose which will fail to prevent regrowth must be much greater than has been believed hitherto.]

The technic of Adamson and Kienbock has been used successfully for many years. I believe that until a practical technic is evolved which will overcome the objections raised by Molesworth and Riddle it is safer to adhere to the technic described by MacKee in his book. Abstractor]

CIPOLLARO, New York

DEFINITION AND ETIOLOGY OF ECZEMA. JOHN T. INGRAM, *Brit J Dermat* 47 502 (Dec) 1935

Ingram expresses the belief that the essential characteristic of eczema is the fact that it is an itching, uniform, pinhead-sized eruption. This reaction is seen both clinically and histologically. The etiology depends on hypersensitiveness of the skin, an external irritant and autosensitization. The hypersensitiveness of the skin is part of the physiologic instability of the patient and may be inborn.

or result from temporary circumstances. A state of nervous instability, malnutrition, an abnormal metabolic state or a toxic state acting locally or generally may occasion the physiologic instability.

The external factor may be any stimulus. In addition there is the factor of autosensitization of the patient to the serum of his own exudates. If the serum is in contact with the skin, an external eruption results. If the serum is reabsorbed into the blood, a generalized eruption may result. Seven illustrations are given.

PANNICULITIS ITS PLACE IN NOSOLOGY H. KEIL, *Brit J Dermat* **47:512** (Dec) 1935

According to Keil, the name "primary panniculitis" refers to the condition in which changes occur in the adipose tissue over wide stretches of the body but no suppuration is present. There are two forms of the condition: the febrile and the afebrile. The febrile form is characterized by crop-like outbreaks of slightly tender subcutaneous nodules on the extremities associated with prolonged irregular fever and constitutional symptoms. The nodules involute, leaving atrophy of the adipose tissue and dimpling of the skin. Cultures of the blood are sterile. The afebrile form is characterized by massive, painless induration of the subcutaneous tissues of the anterior aspect of the trunk, the overlying skin remaining uninvolved.

Keil states that secondary panniculitis may occur coincidentally with erythema nodosum, nodular erythema due to a drug, erythema induratum, Darier-Roussy's sarcoid, lipogranuloma and dermatomyositis (?).

A CASE OF PARAFFINOMA MASON BOLAM, *Brit J Dermat* **47:523** (Dec) 1935

Bolam reports the clinical and histologic observations in a case of paraffinoma occurring in a man aged 36. Lesions occurred on the arms, on the calf of both legs and in the left iliac region at the sites where some drug had been injected nine years before.

The histologic examination revealed a chronic panniculitis without change in the elastic tissue and multiple oil cysts filled with a material which was not double refracting.

Bolam expresses the belief that these nodules may be due to impurities in the substance injected or to a personal susceptibility of the patient to that substance. A brief review of the literature and a photomicrograph are given.

WIEN, Chicago

STUDIES ON INFANTILE ACRODYNIA. I. NOTE ON THE YEARLY AND SEASONAL INCIDENCE E. LEENHARDT and J. BOUCOMONT, *Rev franç de pédiat* **11:265**, 1935

In the course of the last seven years the authors have observed thirty-eight cases of acrodynia. The number has increased yearly, and in 1934 fifteen cases were observed. By far the greatest number occurred in the winter and spring. The authors raise the question as to whether acrodynia is a neurovegetative localization of a banal infection of the respiratory passages. They also cite the hypothesis of Moro that there is hyperexcitability of the vegetative nervous system in the spring, which in certain infants may take the form of acrodynia.

LESLIE, Evanston, Ill [AM J DIS CHILD]

CUTANEOCEREBRAL ANGIOMA J. S. CHARAVIS, *Rev d'oto-neuro-opht* **12:755** (Dec) 1934

Certain cutaneous vascular lesions, such as vascular nevi of the face, may be accompanied by true cerebral angioma. Often they are accompanied by angioma of the retina. These disorders must not be confused with angiogliomatosis of the retina, with atypical Recklinghausen's disease associated with cerebral lesions,

or with pure cerebral angiomatoma without any cutaneous or ocular lesions. A boy, aged 14, presented mucocutaneous angiomatous nevi in the region supplied by the right trigeminal nerve, with homolateral cerebral angiomatoma, there were no signs of a pathologic neurologic process except epileptic attacks and mental dulness, but pronounced calcification of the vascular tumor, syphilitic iridocyclitis in the right eye, and positive reactions to the Wassermann and Hecht tests were present. While the pathogenesis in these cases is not settled, Charamis is inclined to attribute the cause of the diseases in this case to syphilis. Active antisiphilic treatment and high voltage roentgen therapy were applied. If the cerebral complications become menacing, extirpation of the tumor is indicated, in spite of the attendant risks. DENNIS, San Diego, Calif [ARCH NEUROL & PSYCHIAT]

BLASTOMYCOSIS DUE TO SCOPULARIOPSIS BREVICAILIS LUIGI CIARROCCHI, Gior ital di dermat e sif 76 1409 (Dec) 1935

Ciarrocchi reports a case of dermatitis circumscribed to the upper third of the right forearm occurring in a man aged 29. Scopulariopsis brevicaulis var hominis (Brumpt and Langeron) was recovered. The patient had an uneventful recovery as a result of treatment with a salve containing salicylic acid and sulfur. Intradermal tests with fungus extract were positive, and agglutinins were present in the blood serum of the patient. Inoculation of animals gave negative results.

SEASONAL VESICOBULLOUS DERMATITIS PRODUCED BY A BEETLE (PAEDERUS FUSCIPES, FAM STAPHYLINIDAE) A. BACCAREDDA, Gior ital di dermat e sif 76 1423 (Dec) 1935

Baccaredda identified a small beetle (*Paederus fuscipes*) as the cause of a recurrent seasonal vesicobullous dermatitis occurring in small epidemics during the summer and affecting the uncovered parts, especially the face and neck. A similar dermatitis due to a member of the species "fuscipes" has been described as occurring in southern Russia.

PARDO-CASTELLO, Havana, Cuba

A SIMPLE METHOD FOR THE REMOVAL OF TATTOOING JANSON, Dermat Wchnschr 101-894 (July 20) 1935

Janson states that in 1921 he observed that soldiers living in relatively unsanitary surroundings exhibited folliculitis and excoriations from scratching. In several instances he noted the disappearance of tattooing in areas which had been subjected to constant scratching and secondary infection. Subsequently he removed a tattoo from a patient's back by scrubbing the area with a stiff bristled brush, the area being anesthetized with procaine hydrochloride. Three treatments resulted in the disappearance of the tattoo, and according to the author, the cosmetic effect was very good "for a man's back."

EXCRETION OF SODIUM CHLORIDE IN FEBRILE PATIENTS AND ITS IMPORTANCE IN REGARD TO THE SO-CALLED SALT RETENTION IN PATIENTS WITH PEMPHIGUS VULGARIS HUGO WOLFF, Dermat Wchnschr 101 911 (July 27) 1935

From a series of tests of the sodium chloride metabolism, Wolff draws the following conclusions: 1 All toxic febrile patients show a decrease in urinary excretion of sodium chloride. This may be interpreted as a retention of the salt but it is balanced by increased excretion of sodium chloride in the sweat. 2 In patients with a high fever and marked sweating sodium chloride may be entirely absent from the urine. 3 Artificially produced fever causes the same decrease in the salt content of the urine. 4 The length of time before excretion of salt in the urine returns to normal depends on the height and duration of the fever.

Wolff concludes that it is evident that the frequently reported retention of salt in patients with pemphigus is only apparent.

LEUKODERMA FOLLOWING A LATE RECURRENT SYPHILITIC EXANTHEM THOMAS PREININGER, *Dermat Wchnschr* 101:916 (July 27) 1935

Depigmented areas developed on the chest, the labia pudendi and in the intergluteal cleft of a patient with resistant recurring syphilis

OSTEITIS TUBERCULOSA MULTIPLEX CYSTOIDES (JUNGLING) IN A CASE OF LUPUS VULGARIS FRANZ KOCH, *Dermat Wchnschr* 101:919 (July 27) 1935

A case of typical lupus vulgaris associated with osteitis tuberculosa multiplex cystoides is described. Injections of tuberculin produced a flare-up of the cutaneous condition and also pains in the fingers affected by the osteitis

TO WHAT EXTENT DOES THE NECESSARY DURATION OF ANTISYPHILITIC THERAPY DEPEND ON ITS INTENSITY? E ZURHELLE, *Dermat Ztschr* 72:57 (Sept) 1935

Zurhelle has had experience with the short intensive courses of antisyphilitic treatment advocated in Bonn, Germany, and with the longer less intensive courses formerly used in Groningen, Netherlands. He states that the shorter, more intensive courses are as effective, a lower total amount of arsphenamine and bismuth being administered. He therefore makes use of the "maximal treatment" whenever this is practicable. Toxic effects from the medication were no more frequent in patients receiving the intensive than in those receiving the longer courses of treatment.

EROSIVE PLURI-ORIFICIAL ECTODERMOSIS AND ITS RELATION TO ERYTHEMA EYSUDATIVUM MULTIFORME L KUMER, *Dermat Ztschr* 72:62 (Sept) 1935

Under the name erosive pluri-orificial ectodermosis French authors have described an acute febrile disease characterized by the formation of bullae and vesicles on the buccal mucosa and of pseudomembranes. Other mucous membranes are often involved. Cutaneous eruptions in the form of papules, bullae, purpuric or varicelliform lesions are frequently seen. Recurrences occur in most instances. Kumer describes two cases of a disorder that apparently belongs in this classification. He expresses the belief that the dermatostomatitis described by Baader is the same condition and that in both instances the disorder may have been an atypical manifestation of erythema multiforme.

NEW CLINICAL AND EXPERIMENTAL CONTRIBUTIONS TO THE QUESTION OF LYMPHOGRANULOMA VENEREUM H LÖHE and H SCHLOSSBERGER, *Dermat Ztschr* 72:70 (Sept) 1935

Material obtained from a patient with lymphogranuloma venereum was injected into monkeys and guinea-pigs. The infection was carried through a number of generations, and this passage markedly increased the virulence of the virus. Filtration through a Seitz filter caused a considerable decrease in the virulence.

TAUSSIG, San Francisco

CUTANEOUS METASTASES IN THE FIELD OF IRRADIATION OF A PYLORIC CANCER O SCHURCH, *Ztschr f Krebsforsch* 41:47, 1934

There is described a case of pyloric carcinoma in which after operation (without excision) and prophylactic irradiation early cutaneous metastases appeared which were limited to the irradiated area. The phenomenon is directly the opposite of what would be expected from experimental observations. Schurch explains it on the ground of vascular trauma by the irradiation, with establishment of a site of lowered local resistance to tumor implantation.

EGGERS, Omaha [ARCH PATH]

CONTRIBUTION TO EXPERIMENTAL SPOROTRICHOSIS I EXPERIMENTAL INOCULATIONS OF SPOROTRICHUM BEURMANNI (KOBAYASI STRAIN) INTO WHITE RATS AND RABBITS T KOBAYASI, Jap J Dermat & Urol 38 747 (Nov) 1935

Kobayasi reports experimental work on sporotrichosis caused by inoculation of white rats and rabbits with *Sporotrichum Beurmanni* (Kobayasi strain). The clinical observations were reported previously (*Jap J Dermat & Urol* 36 665, 1934) and abstracted in the ARCHIVES (37 648 [Oct] 1935). Another report (*Nagasaki Igakkai Zasshi* 13 1687 [Nov] 1935) is not available at present.

The infective material was inoculated subcutaneously, intravenously into the marginal vein of the ear of rabbits and intraperitoneally. The subcutaneous inoculations resulted in a local abscess consisting histologically of a small central abscess surrounded by a rather narrow middle layer consisting chiefly of histogenic wandering cells or histiocytes of Kiyono (possibly plasma cells) and by an outer layer consisting chiefly of a fibroblastic reaction (granulation tissue).

The intravenous inoculations resulted in so-called sporotrichotic pneumonia, or pulmonary sporotrichosis. This process consisted in the main of initial sporotrichotic embolism (miliary sporotrichotic tubercles) and later caseous pneumonia or pulmonary hepatization. The early embolic lesion consisted of an initial infiltration of the intravascular embolus and surrounding tissues with histiocytes, which later assumed an epithelioid character, and of an outer layer of connective tissue reaction. A few giant cells were intermixed, particularly in the outer zones, and the majority contained fungous bodies and cellular debris and were evidently foreign body giant cells. Yet a few of them did not have inclusions and histologically appeared to be typical Langhans giant cells.

Because of a mistake the intraperitoneal inoculations resulted in some cases in retroperitoneal inoculations, causing a perinephric abscess and pulmonary metastases as described, in other cases the intraperitoneal inoculations were successful and caused an initial intense peritoneal reaction (leukocytic extravasation) and later resorption, intraperitoneal walling off or so-called milkspot (*Langerhans' Trübung*) followed in some instances by eventual resorption. The pathogenic fungus was obtained by culture of material from the lesions and, in the case of animals with metastatic perinephric abscesses, from the heart blood.

In all the lesions the pathogenic fungus could be seen microscopically as a small deeply stained round or oval body with a strongly refractive capsule, measuring from 2 to 3 microns in diameter.

ECZEMATOUS CHANGES IN THE SKIN AND FAT METABOLISM T OZAKI, Jap J Dermat & Urol 38 771 (Nov) 1935

Ozaki studied the total fatty acids, phosphatides (lecithin) and total cholesterol content of the skin in relation to experimental dermatitis produced by croton oil. The total fatty acids were extracted with ether and alcohol, saponified with sodium hydroxide and weighed dry. The phosphorus content of the lecithin substances, ashed with sulfuric acid and fuming nitric acid, was determined by multiplying the theoretical factor 0.054 by the amount of four hundredths-normal sodium hydroxide required to dissolve a precipitate of ammonium phosphomolybdenate. For determination of the cholesterol content the free cholesterol was weighed as a digitonin precipitate, the residual cholesterol ester being then saponified with sodium alcoholate and precipitated and weighed as described for phosphorus. The methods used are those described in Takata's "Biochemical Analysis" (*Shōkwagaki Bunseki*, 1927, p 610), the digitonin method being a modification of the Windaus method (*Ztschr f physiol Chem* 65 110, 1910).

During the acute stage of the croton oil dermatitis in the rabbit the amounts of total fatty acids, phosphatides and cholesterol diminish markedly, they rise to abnormally high values during the subacute stage (nineteenth day) and finally sink gradually back to normal. Tables showing the variations of each constituent in milligrams per hundred grams of skin accompany the article.

The conclusion is that experimental dermatitis exerts an influence on the metabolism of fats.

J W BRENNAN, Chicago

CASE OF ERYTHEMA ANNULARE (LEHNDORFF AND LEINER) J A VAN KRIFKEN, *Maandschr v kindergeneesk* 4:224 (March) 1935

A description is given of a case of the erythema annulare of Lehndorff and Leiner in a girl, aged 7 years, who was admitted to the hospital for the treatment of gonorrheal vulvovaginitis. During her stay in the hospital acute rheumatic fever developed, associated with rheumatic endocarditis and annular erythema.

ONE HUNDRED AND TWENTY CASES OF ERYTHEMA NODOSUM H SANDRA, *Nederl tijdschr v geneesk* 79:13 (Jan 15) 1935

A detailed report is given of one hundred and twenty cases of erythema nodosum, in which examination was made at a consultation office for tuberculous patients. The number of adults was twice that of children. In accord with Wallgren and many other authors, erythema nodosum is considered in most cases to be a symptom of tuberculous infection. The early detection of all patients with erythema nodosum is of great importance for a successful fight against tuberculosis, and the consultation offices should be charged with this task.

HEREDITY OF ALBINISMUS CIRCUMSCRIPTUS J SANDERS, *Nederl tijdschr v geneesk* 79:1245 (March 23) 1935

Three families consisting of seventy-four persons are described, in thirty-nine of whom albinismus circumscriptus occurred on the forehead, abdomen and legs. The anomaly is dominant. The hypothesis of Frassetto regarding the cause of this hereditary deviation is discussed. In the author's opinion, this hypothesis cannot explain the occurrence in all the cases.

PSORIASIS AND MEASLES C H BEEK, *Nederl tijdschr v geneesk* 79:4157 (Aug 31) 1935

Through an investigation of the anamneses of 100 adults suffering from psoriasis and of 100 persons used as controls, it could be proved that in both groups there was a history of measles. This observation is contrary to the opinion that measles protects against psoriasis.

DERMATITIS GANGRAENOSA INFANTUM I COHEN, *Nederl tijdschr v geneesk* 79:5143 (Nov 2) 1935

The description is given of a case of dermatitis gangraenosa in a baby 1 month old, who until ten days after birth had been healthy. In material obtained from a complicating closed cutaneous abscess only *Staphylococcus aureus* was observed. Notwithstanding the age, the progress of the ulcers and the serious general state of the child, recovery was obtained after two months' hospitalization, the most important therapeutic agents being numerous injections of antistaphylococcus serum and daily blood transfusions.

VAN CREVELD, Amsterdam, Netherlands [AM J DIS CHILD]

Society Transactions

CLEVELAND DERMATOLOGICAL SOCIETY

J R DRIVER, M D, *Reporter*

Regular Meeting, Dec 26, 1935

H G MISKJIAN, M D, *Presiding*

INTRACRANIAL HEMANGIOMA WITH HEMIPLEGIA Presented by DR JOHN A GAMMEL

J S, a boy aged 8 years, from the service of Dr Cole and Dr Driver at the Lakeside Hospital, was born with port wine nevus involving the right half of the face and areas on the upper and lower extremities. At the age of 18 months he had a convulsion, this was followed by a spastic hemiplegia on the right side which has persisted, impairing the function of the leg and arm. The child is undersized, has a relatively large head and asymmetry of the face and is mentally underdeveloped. On the right side of the face, on the distal two thirds of the upper extremities and on the legs are areas of port wine nevus. There is marked bony and muscular atrophy of the right upper and of the lower extremities. When the patient walks he drags his right foot. There is generalized weakness of the entire right side. There is moderate ptosis of the right eyelid. The scleras of both eyes are bluish. The pupillary reflexes are normal, the tendon reflexes are present and are apparently normal on both sides in the arms and legs. The tongue protrudes in the midline.

The Wassermann reaction of the blood was negative. The blood cell count and differential counts were normal, the hemoglobin content of the blood was 73 per cent.

A roentgenogram of the skull made in November 1935 showed it to be asymmetrical, presenting a bulge in the right parietal region. There was evidence of thickening of the left parietal bone, which measured 15 mm in thickness. The frontal and occipital bones were markedly thickened. The inner and outer contour of the bones of the skull appeared to be normal. The sutures were well visualized, and their ossification appeared to be normal. The sella turcica appeared to be normal. The sphenoid sinuses were not developed.

DISCUSSION

DR. E W NETHERTON: I had occasion some time ago to look up the association of neurologic lesions with the presence of nevus. I was rather surprised to find that disorders such as the one in this child are not rare. There are cases reported in the pediatric literature. The condition is probably due to a vascular nevus involving the meninges, the hemiplegia being due to hemorrhage.

CEREBROSPINAL SYPHILIS (SYPHILITIC AMYOTROPHY) Presented by DR JOHN A GAMMEL and DR PAUL G REQUE.

J R, a Negro aged 53, from the outpatient department of the Lakeside Hospital, contracted syphilis in 1906 and received little or no antisyphilitic treatment. In March 1935 he was admitted to the Lakeside Hospital because of weakness in his hands of two years' duration. For several months this weakness had also been present in his legs. He complained of an aching sensation in the knees, hips and shoulder. During the past four months the weakness has become

progressively worse and has been associated with moderate stiffness of the elbow joints. The patient is well developed but rather poorly nourished. Marked muscular weakness is demonstrable in both the upper and the lower extremities. All the tendon reflexes are hyperactive. There is no demonstrable sensory disturbance and no ataxia. The Babinski sign is equivocal. Examination of the cranial nerves showed that all were intact. The patient has no difficulty of speech. The pupils are small and fixed to light but react slightly in accommodation. The eyegrounds are normal. There are no physical abnormalities. Urinalysis gave negative results. The blood cell count, the differential count and the hemoglobin content of the blood were normal. The Wassermann reaction of the blood was 2 plus. The spinal fluid was under 100 mm of pressure. The Pandy reaction was negative, the number of cells in the spinal fluid was normal, the Wassermann reaction was 2 plus in 0.5 cc and 4 plus in 1 cc of fluid, the mastoc curve was normal.

A roentgenogram revealed atrophic arthritis in the hands. There was a moderate amount of periostitis about the left elbow, a roentgenogram of the skull showed no abnormalities.

Treatment has consisted of intramuscular injections of thiothymol and bismuth and potassium tartrate and internal administration of potassium iodide. There has been no progress of the disease since treatment was started, but improvement, if any has occurred, has been slight.

DISCUSSION

DR JOHN E. RAUSCHKOLB. In making a differential diagnosis one would have to consider, in addition to syphilis of the central nervous system, the possibility of an alcoholic peripheral neuritis or atrophy associated with pseudopellagra.

DR W. H. CONNOR. Recently at the City Hospital there were two patients whose disorder could be classed in the same group as that of this man. Examinations of the spinal fluid gave results similar to those reported by Dr Gammel and Dr Reque. The response to antisyphilitic treatment has been poor.

DR H. N. COLF. This type of syphilis of the central nervous system is rare and interesting. There is usually an involvement of the lateral columns of the spinal cord. The syndrome is fairly characteristic.

MACULAR ATROPHY OF THE SKIN. Presented by DR H. G. MISKJIAN and DR MAURICE SULLIVAN

CASE 1—L. M., a Negress aged 41, from the service of Dr. Cole and Dr. Driver at the Lakeside Hospital, was first seen in the outpatient department in August 1935, when she complained of a large gumma of the skin of the left forearm, which had healed with scar formation after the institution of antisyphilitic treatment. It was noted at the time of the first examination that the patient had an extensive eruption, chiefly over the back, consisting of rounded atrophic lesions varying in size from that of a split pea to that of a bean. These lesions on palpation gave the impression of a circumscribed loss of elasticity of the skin. The duration of these lesions was indefinite. Biopsy of material from one of the atrophic lesions showed the thickness of the epidermis to be decreased. The papillary pegs were completely flattened. The total thickness of the corium was greatly decreased. There was undulation of swollen connective tissue fibers in the deeper portions. Cellular infiltration in the superior layer was sparse. Elastic tissue fibers were absent.

The Wassermann reaction of the blood was strongly positive. Examination of the spinal fluid gave negative results.

CASE 2—P. S., a Negress aged 33, from the service of Dr. Cole and Dr. Driver at the Lakeside Hospital, had a generalized eruption and some moist perianal sores in 1921. Tests of the blood made at that time gave strongly positive reactions. After antisyphilitic treatment was administered the lesions on the skin healed, leaving scars, which have persisted. Over the entire body but espe-

cially marked over the trunk are numerous round and oval atrophic lesions, they vary in size from 2 to 2.5 cm in diameter, and few are even larger. Some of these lesions present a ballooned appearance, but on palpation they are soft, inelastic and atrophic.

Biopsy showed the epidermis to be flattened in the corium. The connective tissue is edematous. There is a moderate amount of round cell infiltration about the vessels. Elastic tissue fibers are absent.

CASE 3—E. T., a woman aged 49, from the service of Dr. Cole and Dr. Driver at the Lakeside Hospital was admitted to the hospital in March 1935 for hemorrhoidectomy. On examination at that time it was noted that the patient had widely scattered atrophic lesions on the skin. She stated that these had been present for only a few months and that there had been no preexisting inflammatory eruption. On the arms, forearms and shoulders are a few widely scattered irregular and round raised and depressed lesions approximately 1 cm in diameter. The lesions are bluish white and resemble bladder-like formations. On palpation they give the impression of small hernia-like lesions of the skin. The Wassermann reaction of the blood was negative. Biopsy showed a thin layer of stratified squamous epithelium with narrow bands of keratin on its surface. The rete pegs were small and flattened and in some areas were entirely absent. In the corium was dense hyalinized connective tissue with a scarcity of elastic fibers. There were small accumulations of mononuclear cells around the smaller vessels of the corium.

DISCUSSION

DR. BENJAMIN LEVINE: I was able to elicit a history of varicella in two of the cases, I believe that in these the atrophy is more or less typical of that which follows this disease and that it does not represent true macular atrophy. The condition in the other case, however, seems to be characteristic of syphilitic macular atrophy.

DR. H. J. PARKHURST, Toledo, Ohio: In the two Negro patients the macular atrophy following secondary syphilis seems quite apparent to me. The eruption exhibited by the third patient is characteristic of the multiple benign tumor-like new growths of the skin described by Schweninger and Buzzı. The significance of the history of erythematous papules or nodules preceding the lesions, however, is not clear.

DR. H. N. COLE: The two Negro patients present macular atrophy secondary to syphilis. This disorder is rare. The other patient's disorder corresponds to that described by Schweninger and Buzzı. I do not believe that varicella enters into the picture in any of these cases. Varicella produces a scar, while these patients exhibit atrophy.

DARIER'S DISEASE Presented by DR. JOHN A. GAMMEL

J. S., a Yugoslavian aged 40, has had an eruption on the back for fourteen years. Two weeks ago tonsillectomy was performed, after this a pruritic erythematous eruption appeared on the central portion of the chest. The patient's general health has been good. The eruption involves the anterior and posterior aspects of the chest, the axillae and the pubic region. The lesions are small light brown follicular papules. Over the chest there is a more acute process superimposed, the latter consists of reddish papules and a few pustules with excoriations. There are no other abnormalities. The Wassermann reaction of the blood was negative.

Biopsy revealed the histologic picture of Darier's disease.

DISCUSSION

DR. H. N. COLE: This is a rather interesting and unusual manifestation of Darier's disease. It is not unusual for patients with such disorders to have a secondary infection, which would explain the acute infectious eczematoid dermatitis present on the chest.

PIGMENTED CICATRIZING NEVUS OF THE NOSE Presented by DR E W NETHERTON

M D, a man aged 49, states that about ten years ago a small dark scaly lesion developed on the right side of the nose, half-way between the inner canthus of the eyes and the ala of the nose. There has never been any ulceration. The spot has gradually enlarged fairly evenly in all directions, and the progressing margin has always been slightly raised and hyperpigmented, while the central portion of the lesion has remained depressed, depigmented and scarred. There has always been a small nodule at the site of the original lesion. At present there is on the right side of the nose and on the adjacent portion of the right cheek an irregular, well defined, noninflammatory lesion, in approximately the center of which there is a nodule the size of a split pea with a small area of melanotic pigmentation on its surface. The greater part of the lesion is smooth and depressed below the normal surface of the skin and consists of a depigmented atrophic-like scar. The margins of the lesion are raised and hyperpigmented. In places this raised margin is threadlike, while along the ala of the nose it is much thicker, somewhat verrucous and more hyperpigmented.

The blood count showed 4,130,000 red cells, 6,800 white cells and 78 per cent hemoglobin. The sugar content of the blood was 118 mg per hundred cubic centimeters. The Wassermann and Kahn tests of the blood and urinalysis gave negative results. A biopsy showed a moderate keratosis with enlargement of the rete pegs and dermal papillae. There was a relatively large amount of melanin in the pigment in the dermis. There were a few small rather cellular areas in the dermis, associated with melanin pigment suggestive of nevus tissue. The cells did not appear to be actively proliferating. There was no evidence of neoplasm arising from the epidermis.

Grenz ray therapy has been used without any results or apparent change in the lesion. A portion of the margin of the lesion was cauterized with the electric cautery.

DISCUSSION

DR H J PARKHURST, Toledo, Ohio. The clinical appearance of the lesion impresses me as being that of basal cell epithelioma, and from examination of the section I thought that this impression was justified.

DR H N COLE. It would be interesting to make another biopsy. From examination of the section I was not willing to make a diagnosis of nevus. There were some characteristics of lupus erythematosus and evidence of scar formation, and I believe that it is not unheard of to find a certain amount of pigment in the papular type of lupus erythematosus. Clinically the lesion suggests epithelioma.

DR JOHN E RAUSCHKOLB. I favor a diagnosis of basal cell epithelioma and suggest that attempts be made to determine the characteristics of the pigment by means of the dopa reaction.

DR E W NETHERTON. On first examination the lesion impressed me as being a basal cell epithelioma with pigmentation. However, the possibility of a pigmented melanoma suggested itself. I shall attempt to get a deeper specimen for biopsy.

NOTE—A second biopsy was made and showed a pigmented basal cell epithelioma. The base was treated with radium.

CONGENITAL SYPHILIS, ENLARGEMENT OF THE STERNAL END OF THE CLAVICLE Presented by DR H G MISKJIAN

R N, a girl aged 16, until three years ago, had frequent convulsions. These were supposed to be due to chronic pyelitis. The patient had pertussis and diphtheria at the age of 7 years, measles and pneumonia at the age of 8 years, a supernumerary digit was excised when she was 3 years old. She has not had scarlet fever or rheumatic fever. She has always been sickly, in infancy she had fre-

quent gastro-intestinal upsets, and in childhood she was frail and nervous. According to the mother there has always been some disproportion in the sternoclavicular region, the left portion being larger than the right.

During the past year, especially during the last three months, the mother has noted a fairly rapid enlargement in the left portion of the sternoclavicular region. At present the patient is fairly well developed, nervous and irritable. The sternal end of the left clavicle is the seat of a fairly extensive diffuse hard but not bony swelling. There is no change in the color of the overlying skin. A scar on the surface represents an incision resulting from excision of a biopsy specimen. The surface of the swelling is raised about 1.5 cm above the surface. The Wassermann reaction of the blood was 4 plus. Red and white blood cell counts were normal. Urinalysis gave negative results. A roentgenogram made on April 20, 1935, showed that the sternal end of the left clavicle was 2.5 cm in width while that of the right was 1.5 cm. Cartilage could not be visualized. There was no evidence of destruction or proliferation of bone. There are bilateral cervical ribs, the left being larger than the right. These arise from the eighth cervical vertebra. Biopsy showed masses of hyaline cartilage surrounded by dense fibrous connective tissue. The cartilage cells were sparse in a normal hyaline matrix. There was no hyperplasia and no atypical aggregations of cells. The capsule of the mass was thick and densely fibrous. There was no evidence of tumor formation.

Five hundred roentgens of radiation filtered with 2 mm of aluminum was administered to the keloidal scar on Aug. 14, 1935. After ten injections of an insoluble preparation of bismuth tartrate and ten injections of mapharsen in doses of 0.03 Gm. each a slight decrease in the size of the mass was noted.

DISCUSSION

DR. H. N. COLE: Periostitis and formation of gumma at the sternal end of the clavicle are fairly common in both congenital and acquired syphilis. The occurrence of supernumerary digits has also been reported in congenital syphilis.

FOX-FORDYCE'S DISEASE Presented by DR. H. G. MISKJIAN and DR. MAURICE SULLIVAN

CASE 1—H. S., a Negress aged 25, from the service of Dr. Cole and Dr. Driver at the Lakeside Hospital, has an itchy eruption in the axillae and in the perineal and pubic regions. The patient is nervous and introspective and is much distressed over her condition. She says that the itching is almost continuous but that it is much worse during menstruation and when she is under a nervous strain. She complains of backache. There is a chronic vaginal discharge. The eruption consists of discrete follicular papules in the axillae, over the mons veneris and around the nipples; there is no surrounding inflammatory reaction. The eruption is slightly scaly. There is almost complete loss of hair due to scratching.

Roentgenograms of the skull revealed increased sagittal markings. The basal metabolic rate was -12 per cent. Urinalysis gave negative results. The blood cell count showed a normal hemoglobin content and a normal number of red cells, the white cells numbered 5,000. The differential count was normal. The Wassermann reaction of the blood was negative. Examination of the stools gave negative results. The dextrose tolerance test revealed greatly increased tolerance, the sugar content of the blood being 67 mg. per hundred cubic centimeters and a peak of 74 mg. occurring after the dextrose was given.

The results of biopsy were reported as follows. The epidermis showed a fairly marked acanthosis. The interpapillary projections were elongated and thickened. In the middle portion of the section two interpapillary pegs were much larger and deeper than the others. These showed a certain degree of spongiosis. On the outer surface of the epidermis there was a fairly wide area which stained intensely red and showed parakeratosis. Between the upper cells of the malpighian layer and the deeper portions of the parakeratotic area there was some exudation in which fragments of migratory cells were present. On other parts

of the surface one or two small horny plugs were present. The papillary layer of the corium was characterized by a feeble staining quality. The papillae were widened, and many contained dilated blood spaces. Around the aforementioned interpapillary projections there were extensive, though loose, lymphocytic infiltrations along with a number of thick connective tissue cells. A few lymphocytes had forced their way into the epidermis. In the reticular portion of the corium were limited areas of loose perivascular infiltration. A large number of coil glands cut at various angles were seen underlying the corium. These were of the apocrine type, they were perhaps somewhat dilated and at various stages of activity. There was hardly any infiltration around these coils. Much more of infiltration was seen around the hair follicles.

The following therapeutic measures have been used without much apparent result: roentgen irradiations, administration of thyroid, corpus luteum extract and ovarian extract and application of antipruritic ointment.

CASE 2—I W., a Negress aged 15, presented herself at the outpatient department of the Lakeside Hospital because of a severely pruritic eruption in the axillae of six months' duration. There has been little or no change in the appearance of the eruption during the past three years. Approximately six months ago the pruritus suddenly stopped, and there has been no recurrence of it. In the axillae is a marked papular eruption. The papules are firm and are arranged in parallel lines suggesting planes of cleavage. There is a sparse growth of hair. A few lesions are present also in the pubic region. Urinalysis gave negative results. The blood cell count showed 4,300,000 red cells, 3,800 white cells and 78 per cent hemoglobin. The differential count was normal. The curve for dextrose tolerance was as follows: during fasting, 69 mg of sugar per hundred cubic centimeters of blood, thirty minutes after administration of dextrose, 67 mg, one hour after administration of dextrose, 77 mg, and one and one half hours after administration of dextrose, 66 mg. The basal metabolic rate was -20 per cent.

Results of a biopsy were reported as follows. The epidermis showed acanthosis and some degree of spongiosis. The interpapillary projections were surrounded by a lymphocytic infiltrate. The vessels in the corium showed a slight perivascular infiltration. There was an infiltration of exudative cells into the cutis, composed of monocytes, polymorphonuclear eosinophils and neutrophils. There were a number of dilated coil glands of the apocrine type.

In 1933 the patient received 200 roentgens of filtered radiation three times at intervals of two weeks and obtained considerable relief for a few months.

CASE 3—M C., a girl aged 15, has an eruption which started two years ago with intense pruritus in the axillae and pubic areas. It consists of firm grayish to violaceous follicular papules, some of which show a slight central depression. The lesions are quite numerous and closely packed and show a tendency to arrangement in parallel lines. Urinalysis gave negative results. The blood cell count showed 3,000,000 red cells, 4,200 white cells and 65 per cent hemoglobin. The differential count was normal. The Wassermann reaction of the blood was negative. The basal metabolic rate was -33 per cent. The curve for dextrose tolerance was as follows: during fasting, 77 mg of sugar per hundred cubic centimeters of blood, thirty minutes after administration of dextrose, 121 mg, one hour after administration of dextrose, 93 mg, and two hours after administration of dextrose, 144 mg.

Results of biopsy were reported as follows. The epidermis was slightly thicker than normal. There were some new blood vessels in the corium with perivascular infiltration of lymphocytes. Edema and infiltration were observed around several of the sudoriferous glands. There was one lobular collection of hyperplastic and dilated sudoriferous glands (apocrine glands).

The patient has received 0.03 Gm of thyroid three times a day and pills of ferrous carbonate U S P. The basal metabolic rate three months after institution of therapy was -2 per cent. She also received three doses of radiation consisting of 150 roentgens filtered with 1 mm of aluminum at three week intervals. No improvement has resulted from this therapy.

DISCUSSION

DR E W NETHERTON It is interesting to note that the basal metabolic rate was reduced in all three cases. I have recently observed a case of Fox-Fordyce's disease in which hyperthyroidism was present. The absence of itching in one patient is also noteworthy. Dr Miskjian and Dr Maurice Sullivan are to be congratulated on presenting three patients with this interesting disorder at one meeting.

J R DRIVER, M D, *Reporter*

Regular Meeting, Jan 23, 1936

H G MISKJIAN, M D, *Presiding*

ACANTHOSIS NIGRICANS Presented by DR MAURICE SULLIVAN

R G, a Jew aged 20, from the service of Dr Cole and Dr Driver at the Lakeside Hospital, had the usual diseases of childhood but has never had any serious illness. He has had acne for several years. In 1920 he was treated in the outpatient department for a condition described as eczema. In 1926 a diagnosis of seborrheic dermatitis of the psoriasisiform type was made. In 1928 he was treated again for seborrheic dermatitis. His present cutaneous trouble started early in 1933, as a more or less generalized eruption, and has gradually become more extensive, affecting especially the lower part of the abdomen, the genitalia, the thighs, the right axilla and the upper portion of the back. The lesions are in various stages of development, some are small and others large. The right axilla is completely filled with one crusted lesion. Some lesions have healed, leaving soft white scars with a brownish pigment at the border. Many of the earlier lesions consist of small hyperpigmented papules. In the flexor areas there is some discharge of seropurulent material. Over the face and upper portion of the back the eruption is of an acneiform type. The Wassermann reaction of the blood was negative. Examinations of the blood revealed no abnormalities, cultures for fungi gave negative results. Examination of the stools disclosed no parasites. A roentgen examination of the gastro-intestinal tract showed nothing of importance. Biopsy showed the epithelium to be rather markedly hyperkeratotic, thicker than normal and somewhat irregular. There was pleomorphism of the cells in the epidermis and irregularity of the basal layer. There was no invasion and no disturbance in pigment distribution. In several areas there were dense cells of polymorphonuclear leukocytes associated with focal tissue necrosis and generally with little fixed tissue reaction. There were several sharply circumscribed areas in which the normal corium had been replaced by collections of epithelioid cells, and among these were many small giant cells, which were multinucleated and contained peripherally disposed nuclei. There was no caseation necrosis and no tubercle formation.

DISCUSSION

DR J R DRIVER Clinically the condition is highly suggestive of acanthosis nigricans. However, the lack of pigment in the biopsy specimen is against this diagnosis, and it may be that the disorder is simply an unusual manifestation of seborrheic eczema with secondary infection resulting in the unusual scarring.

DR H N COLE The picture is rather unusual. The localization of the lesions is the same as in acanthosis nigricans. I believe that further study will prove this diagnosis to be correct.

BLUE NEVUS Presented by DR JOHN E RAUSCHKOLB

C T, a woman aged 22, from the service of Dr Cole and Dr Driver at the City Hospital, has had a lesion on the left cheek near the temporal area since

birth It is speckled and bluish green, and from it grow numerous coarse hairs By transillumination from the mouth the lesion is plainly visible in the cheek, manifesting itself by numerous dilated and connected vessels which do not pulsate Deposits of an apparently increased pigment are present in the skin

DISCUSSION

DR. G. W. BINKLEY I believe that this lesion is an example of the blue nevus of Jadassohn due to an infiltration of pigment cells rather than to vascular change

DR. JOHN E. RAUSCHKOLB I was of the opinion that it was a blue nevus and that is why I presented the patient I am wondering, however, about the possibility of malignant degeneration, and for that reason I hesitate to remove material for a biopsy

DR. H. N. COLE Blue nevi are said not to degenerate

DR. J. R. DRIVER The resemblance of this lesion to the type of accidental tattoo seen in coal miners is striking I agree, however, with the diagnosis of blue nevus

NECROBIOSIS LIPOIDICA DIABETICORUM Presented by DR. W. H. CONNOR

E. G., a Jewess aged 39, from the service of Dr. Cole and Dr. Driver at the City Hospital, has been treated in the outpatient department since 1930 for obesity, thyroid and ovarian hypofunction and diabetes mellitus In October 1932 she noticed an eruption on the left breast, consisting of two coin-sized plaques, another lesion appeared over the metacarpophalangeal joint of the index finger of the left hand Some lesions are located on the lateral aspect of the right leg, and there is another lesion just below the right knee on the anterior surface In 1935 another lesion appeared on the right forearm The earlier lesions have increased slightly in size The lesions vary from 4 to 7 cm in diameter They are slightly raised and infiltrated and have a violaceous, dull brownish red border The central portion of the involved area is markedly xanthochromic and shows some telangiectasia

The Wassermann reaction of the blood was negative The patient's weight averages 250 pounds (113.4 Kg) The sugar content of the blood ranges from 147 to 266 mg per hundred cubic centimeters The cholesterol content ranges from 142 to 199 mg

A biopsy was reported on as follows The epidermis showed occasional mild hyperkeratosis, moderate intercellular edema and some flattening of the rete pegs The vessels in the papillary layer were slightly dilated, and the collagen was slightly increased The blood vessels throughout the corium showed thickened walls, narrow lumens and collars of small round cells There were foci of necrobiotic changes with degenerated homogeneous-appearing fibrous tissue and infiltration with fibroblasts There were various large and small round cells and spaces which by special stains were shown to be filled with fat There was also an abnormal content of fat in the degenerative connective tissue Treatment has consisted of a rigid diabetic diet and administration of insulin The sugar content of the blood became normal, but there was little or no change in the cutaneous lesions

DERMATITIS EXFOLIATIVA AND CATARACTS DUE TO DI-NITROPHENOL Presented by DR. J. M. HITCH and DR. W. F. SCHWARTZ

The patient is from the service of Dr. Cole and Dr. Driver at the City Hospital A complete report of this case appeared in *The Journal of the American Medical Association* (106:2130 [June 20] 1936)

DISCUSSION

DR. I. L. SCHONBERG I had an opportunity to see this patient when the disorder first started The lesions at that time were located generally over the body, but the eruption was not universal It closely resembled seborrheic eczema. She

was hospitalized at the Mount Sinai Hospital, but in spite of treatment the eruption continued to spread, and she was then transferred to the City Hospital

DR. H N COLE This case, I believe, is unique in that it is the first that has been reported of an exfoliative dermatitis developing after the ingestion of di-nitrophenol For this reason I think that the case is worth reporting more completely

LYMPHOBLASTOMA OF THE MYCOSIS FUNGOIDES D'EMBLEE TYPE Presented by
DR W H CONNOR

C G, a policeman aged 39, from the service of Dr Cole and Dr Driver at the City Hospital, states that in December 1934 he began to suffer from a nasal discharge of a seropurulent type The nose became swollen on the right side After roentgen treatment totaling 1,500 roentgens given in divided doses there was marked improvement, and the patient returned to his work for five weeks The process then recurred The Wassermann reaction of the blood was negative, and a therapeutic test consisting of eight injections of neoarsphenamine resulted in no improvement On July 1, 1935, the right side of the nose was incised externally and the right antrum was opened A biopsy made at that time at the Huron Road Hospital was reported to show transitional cell carcinoma The operative wound refused to heal, and an extensive granulating ulcer resulted On July 29, 1935, the patient was admitted to the City Hospital At that time the temperature, pulse rate, respiratory rate and blood pressure were within normal limits Examination showed that there was no pathologic involvement below the neck The cervical lymph nodes were slightly enlarged The nose was approximately twice the normal size, a disproportionate increase being present on the right side There was a ragged ulcer about 2 cm in diameter The nares were practically closed by edema and seropurulent discharge Both upper middle incisors were absent, and in the socket of the right middle incisor there was a sinus leading to the right antrum In the midline of the hard palate, 2 cm posterior to the front teeth, there was a perforating ulcer surrounded by granulations and exuding purulent material

Urinalysis gave negative results Complete examination of the blood disclosed no abnormalities other than a progressive secondary anemia Repeated Wassermann and microscopic precipitation tests for syphilis were negative A test with tuberculin was positive with a 1 100,000 dilution, a 1 1,000,000 dilution gave a negative reaction Repeated examinations, cultures and smears for fungi gave negative results Nonhemolytic streptococci, Staphylococcus albus and Staphylococcus aureus were cultured from the pus Bacillus mallei was never found From July until January the following progress was noted On the left thigh several firm, erythematous nodules in a circinate arrangement developed, ulceration, sloughing and periphereal enlargement followed On both cheeks firm indurated nodules developed, these started as small lesions and increased to the size of a dollar or larger, showing sharply demarcated borders and superficial ulceration The lesion on the nose progressed after temporary improvement had resulted from roentgen treatment in fractional doses averaging a total of 3,000 roentgens

Several specimens for biopsies were taken from new lesions, from the older ulcers and from a lymph node removed from the groin The following diagnoses were based on these examinations nevocarcinoma, lympho-epithelioma, transitional cell epithelioma, chronic granulation tissue, and lymphoblastoma The last diagnosis was based on examination of the lymph node In November 1935 the left ankle became markedly swollen Roentgenogram of the ankle showed a line of diminished density at the epiphysis, this was diagnosed as osseous atrophy In addition to roentgen therapy the patient received injections of foreign protein, intravenous injections of metaphen, local applications, etc

DISCUSSION

DR R E BARNEY The disorder is unusual, and I believe that it is mycosis fungoides d'emblee I recall that in Dr Keim's monograph on lymphoblastoma there is a report of one case of mycosis fungoides in which the first lesion appeared in the mouth, later lesions developed on the body

DR J R DRIVER When the patient first presented himself at the hospital the lesions were limited to the palate and nose. At that time the question of mixed tumor presented itself. I was of the opinion that this lesion, which presented a microscopic picture of lympho-epithelioma and transitional cell carcinoma, had originated as a mixed tumor. However, subsequent biopsies from a metastatic lesion in a lymph node in the groin make the diagnosis of lymphoblastoma more likely.

DR JOHN E RAUSCHKOLB It has been interesting to follow the course of the disorder while the patient was in the hospital. When the nodular lesions of an erythematous type appeared on the thigh they resembled erythema multiforme or erythema nodosum. Examination of material from one of these lesions at that time revealed only chronic inflammatory tissue. I was of the opinion that this manifestation was a toxic erythema resulting from absorption of degenerative neoplastic tissue on the face following irradiation.

DR H N COLE My associates and I have been following this case for several months. There have been many conflicting and confusing factors. At times the clinical appearance of the lesion was that of a syphiloderm. However, at present from the clinical and from the pathologic evidence I believe that the disorder is a lymphoblastoma of the mycosis fungoides d'emblee type.

NOTE—During almost his entire stay in the hospital the patient became progressively worse. He died on Feb 9, 1936, of bronchopneumonia. A brief résumé of the autopsy observations is as follows. The disease was generalized, lesions being present on the skin, in the lungs, in the left testicle and in the lymph nodes. The primary lesion originated in the mucosa of the nose. The diagnosis of lympho-epithelioma based on microscopic interpretation of two intermingling cell types resulted from the mistake of considering what were really degenerated epithelial cells as lymphoid cells. Microscopic studies from the metastatic lesion showed the process to be lymphosarcoma.

NEUROTROPHIC LESIONS ON THE RIGHT SIDE OF THE FACE FOLLOWING THROMBOSIS OF THE LEFT POSTERIOR INFERIOR CEREBELLAR ARTERY Presented by DR W H CONNOR

G W, a man aged 50, from the service of Dr Cole and Dr Driver at the City Hospital, has been suffering from diabetes mellitus and a hypertensive vascular disease. In November 1934 while he was in bed, the patient awoke perspiring profusely, he complained of numbness of the left side of the face and was unable to stand. A few days later vesicles appeared on the lips and on the left cheek, these began to crust and scale, then they healed, leaving atrophic scars. At this time some of the lesions on the cheek have not entirely healed, they have been extremely chronic. Clinically they resemble lupus erythematosus.

Neurologic examination revealed a slow, coarse, clockwise rotary nystagmus when the patient looked to the left and a fine, rapid lateral nystagmus when he looked to the right. There was sensory impairment to light touch and pinprick in the entire left side of the face excepting a small area at the angle of the mandible. There were slight weakness of the left lower portion of the face and a moderate degree of deficiency of hearing in the left ear. There was marked ataxia of the legs, but no definite localization of this ataxia to either side could be demonstrated. There was impairment in sensation to pinprick in the left leg. In the opinion of Dr R E Stout of the neurologic department, these findings represent a thrombosis of the posterior inferior cerebellar artery or cerebellar apoplexy.

DISCUSSION

DR W H CONNOR This patient has been under observation for quite a long time now, and my co-workers and I are indebted to the neurologic department for finally clearing up the diagnosis. At different times the lesions have been considered to be blastomycosis, lupus erythematosus, bromoderma or iododerma. All attempts to prove any of these diagnoses were unsuccessful. A biopsy from one of the lesions simply showed a certain amount of hyperkeratosis, acanthosis and mild chronic inflammation.

SAN FRANCISCO DERMATOLOGICAL ASSOCIATION

JOHN M. GRAVES, M.D., *Secretary*

Jan 24, 1936

C. J. LUNSFORD, M.D., *President*

BULLAE IN SCLERODERMA Presented by DR H. J. TEMPLETON, Oakland, Calif

Mrs W was presented before this society in April 1935 (ARCH DERMAT & SYPH 33 571 [March] 1936) because of an eruption which consisted of bullae superimposed on patches of scleroderma. A factitious dermatitis was also considered at that time. The condition has persisted to date. The section which is shown is suggestive but not typical of scleroderma. The patient states that she has not taken or applied any drugs.

DISCUSSION

DR H. J. TEMPLETON, Oakland, Calif For approximately two years this patient has suffered from lesions which developed slowly, beginning as indurated areas from the size of a dime to that of a quarter. The lesions which I have observed are ivory colored and violaceous at the border. That is the first stage. In the second stage extensive bullae such as the patient exhibits at present form over the lesions. Hemorrhage occurs into the bullae. The next stage can be seen in the lesion over the sternum and consists of a drying and crusting of the bullous lesion. The last stage, exhibited in the lesion in the left scapular region, consists of atrophy.

The patient states that the bullous stage at times lasts for two to three months.

I believe that the pathologic picture is compatible with scleroderma, as evidenced by swelling of the individual collagen fibers and thickening of the whole collagen layer. There are two types of bullous formation—one subcorneal and one in the papillary layer.

DR A. E. INGELS It seems to me that there is nothing in the picture that suggests scleroderma. The skin is soft and pliable. The whole lesion can be lifted up without great difficulty. Moreover, I should say that the pathologic picture is against scleroderma. There is formation of myxoma-like cells beneath the basal layer. This does not fit in with scleroderma. Without sections stained for mucin and amyloid a diagnosis cannot be made. I would hesitate to classify the lesions before seeing the results of differential staining, I should wish to see not only sections stained with hematoxylin and eosin but also sections stained for mucin and amyloid as well as for connective and elastic tissue.

DR H. J. TEMPLETON, Oakland, Calif I have observed two cases of amyloid degeneration of the skin. In neither of them was the appearance like that exhibited by this patient, it more closely suggested patches of lichen simplex chronicus.

DR G. V. KULCHAR The section I saw tonight was compatible with a diagnosis of an early stage of scleroderma. Edema is frequently a feature of the early stage of scleroderma, and there is only a short step from edema to bullous formation. The occurrence of bullae in cases of scleroderma is rare but has been reported.

DR A. E. INGELS How could the presence of myxomatous cells in scleroderma be explained? That association has never been reported.

DR N. N. EPSTEIN I think that clinically the lesions before the appearance of the bullae could well be scleroderma. I disagree with Dr Ingels that the upper layer is myxomatous. This tissue suggests the formation of young connective tissue. I should like to see other slides and stains for confirmation.

MYCOSIS FUNGOIDES Presented by DR N. N. EPSTEIN and DR H. J. TEMPLETON, Oakland, Calif

Gus S., aged 48, is presented to show the effect of fever therapy in mycosis fungoides. He has been presented before this society previously. The histologic picture is typical of mycosis fungoides.

The eruption began in 1929 and has gradually progressed until it is now in the ulcerating tumor stage

Therapy has consisted of roentgen radiation as needed Arsenic was administered in 1931 in the form of solution of potassium arsenite Two intravenous injections of typhoid-paratyphoid vaccine were given in 1931, with no benefit Intramuscular injections of ethyl chaulmoograte administered for two months in 1935 produced no improvement In December 1935 the patient was referred to Dr N N Epstein for fever therapy To date he has received six treatments of five hours each, during which time his temperature was elevated to 40 C (104 F) for thirty hours Fever was induced by the blanket pack method

DISCUSSION

DR N N EPSTEIN Recent reports on the use of fever in mycosis fungoides indicate that fever does have some effect on the course of that disease The results are certainly not startling, but something does happen to the process that seems to reduce the activity The lesions become less red, and tumors have even been known to disappear My co-workers and I have tried to use fever therapy before in cases of mycosis fungoides by attempting to inoculate the patients with erysipelas, but we were unsuccessful We also attempted to produce fever by diathermy, but severe burns resulted Now we have a method of wrapping the patient in blankets and furnishing heat from an external source, which raises the temperature to the desired height This man has tolerated the treatment very well When the patient comes for treatment now he walks into the hospital, and he is quite well as far as strength and weight are concerned, but I do not think that anything except some relief can be expected from the treatment

I do not think that his tumors have changed There are areas on his legs that become paler after treatment He is more comfortable His feet are softer

The use of malaria suggests itself I believe, however, that malaria is too debilitating to use on a patient in this state

DR H J TEMPLETON, Oakland, Calif This case proves that itching is not necessarily a feature of mycosis fungoides

DR N N EPSTEIN Dr W J Kerr has tried several times to inoculate erysipelas, but he has been unable to transmit the disease

DR MERLIN MAYNARD, San José, Calif What method of inoculation was used?

DR N N EPSTEIN Serum from bullae was injected intradermally

DETROIT DERMATOLOGICAL SOCIETY

G WARREN HYDE, M D, *Recorder*

Jan 21, 1936

LOREN W SHAFFER, M D, *President*

A CASE FOR DIAGNOSIS (RHINOPHYMA-LIKE ENLARGEMENT OF THE NOSE, SARCOID?) Presented by DR THOMAS H MILLER

R C, a Negro aged 30, married, born in Georgia, complains of enlargement of the tip of the nose The patient's father, mother, wife and children are living and well

The patient was first seen in 1933, at that time he had a generalized lymphadenitis A diagnosis of tuberculosis was made, being based on the results of biopsy There was no evidence of pulmonary tuberculosis He also presented a bluish red lesion on the nares which had appeared after squeezing of a pimple A diagnosis of rosacea was made, that of an angiolupoid was also considered

The patient was not seen again until today. There is a large bluish red infiltrated soft and bulbous lesion at the tip of the nose with rather indistinct borders which fade into the normal skin. No atrophy, ulceration or apple jelly nodules are present. Enlarged venules course over the surface of the involved area. No tenderness or inconvenience is associated with the disorder.

The patient states that after he was last seen, while he was working outside on a cold day the nose suddenly became enlarged and that it has remained about the same up to the present time.

DISCUSSION

DR JOHN RAUSCHKOLB, Cleveland. I think that the disorder is sarcoid. I believe that a biopsy, roentgen examination of the chest and tests with graded dilutions of tuberculin would help in establishing the diagnosis.

DR HARTHER L. KEIM. It seems to me that this lesion is not simply a dilatation or a hypertrophy of the glands but rather a granulomatous mass, and I believe that a biopsy might show some evidence of tuberculosis. I think that all the members have seen such lesions in Negroes. I do not recall having seen any as extensive as the tumor of the nose exhibited by this patient, but the lesions are often associated with changes in the bones of the fingers, and I suggest that roentgenograms of the hands be made.

PROF. FRANZ BLUMENTHAL, Ann Arbor, Mich. I agree with Dr. Rauschkolb's diagnosis.

LICHEN PLANUS SCLEROSUS ET ATROPHICUS (HALLOPEAU) Presented by DR CYRIL K. VALADE.

A. B. J., a man aged 32, married, born in the United States, states that in 1932 an eruption appeared on the left flank, spreading to the right flank, then to the back and later to the extremities. The patient has experienced no sensations referable to the cutaneous disorder.

There are atrophy and flat-topped white papules. The lesions are both discrete and grouped to form plaques. In the large areas small papules may be seen along the edges. The lesions grouped on the left wrist are glistening pearl-like striated papules. Some are elevated, and all are firm to the touch. The large atrophic areas are fawn colored. There is plugging of the follicles and of the pores.

The sections show at one end a bandlike infiltrate of mononuclear cells such as is commonly seen in lichen planus, but the other changes associated with lichen planus, particularly increase in the granular layer, are not evident. The remainder of the section shows a markedly atrophic epidermis, and under this the papillary body is distinctly sclerotic.

DISCUSSION

DR B. F. BARNEY, Ann Arbor, Mich. I was not sure of the diagnosis. The disorder is probably some variety of morphea. At first I did not notice the needle-like plugging, but on repeated examination I did find such plugging on the wrists, and I think that the diagnosis made by the presenter is justified.

DR GEORGE H. BELOTE. I examined the microscopic sections before I saw the patient. I thought that the slide had some of the characteristics of ordinary lichen planus. However, there were also areas of distinct sclerosis in the section, particularly in the upper third of the corium, and as far as I know it is not common for lichen planus sclerosus et atrophicus of the Hallopeau type to produce the sort of infiltrate exhibited by this patient. Ordinarily if any infiltrate is present in that condition it is deeper than in this section, and consequently in my report to Dr. Valade I said that there was some question in my mind as to whether the disorder was true lichen planus of the Hallopeau type or lichen planus with atrophy.

After looking at the eruption I am still undecided. On account of the infiltrate, however, I favor the diagnosis of lichen planus with atrophy more than that of the true lichen planus atrophicus et sclerosus of Hallopeau.

DR HARTHER L. KEIM. I think the disorder is a borderline condition. In the current year-book this sort of condition is grouped under white spot disease.

TUBERCULID Presented by DR ROBERT C JAMIESON

M A K, a woman aged 22, single, unemployed, was presented in December 1934

DISCUSSION

DR GEORGE H BELOTT The nodules on the face are rather deep-seated, they are purplish and have a doughy feel The appearance suggests paraffinoma Dr Shaffer suggested the diagnosis of sarcoid when the patient was presented in 1934 A few months later she appeared at the clinic at Ann Arbor, Mich, and a biopsy was made The section suggested tuberculosis The patient has since been treated by Dr Jamieson, with the result that the infiltration has practically disappeared but there is marked scarring

DR ROBERT C JAMIESON I presented the patient in order to show the results of roentgen treatment of paraffinoma I saw her after the diagnosis of tuberculosis had been made at Ann Arbor, Mich, and more as an experiment than because I expected definite results I gave her some small doses of filtered roentgen rays After two or three treatments the normal contour of the cheeks appeared, the swelling disappeared, and the improvement progressed until the present stage was reached There is a slight atrophy of the subcutaneous areas in certain places

DR LOREN W SHAFER What amount of roentgen rays was used and what was the individual dose?

DR ROBERT C JAMIESON The doses were small and were administered at weekly intervals I cannot recall offhand exactly how much radiation was given

DR A R WOODBURN, Grand Rapids, Mich There are two little scaly areas on the nose that look like lupus erythematosus I do not believe that those lesions were present when the patient was seen before

DR ROBERT C JAMIESON I think that they were present at the time and are practically unchanged

REPORT ON A CASE PREVIOUSLY PRESENTED DR ARTHUR E SCHILLER

A patient was presented last month with the diagnosis of hatband dermatitis The suggestion was made that the disorder might be lupus erythematosus or an eruption due to phenolphthalein The patient was given phenolphthalein, and there was no flare-up of the eruption, two patch tests with a piece of the hatband made at different times produced a marked reaction on the arm It was hoped that the patient would come today because both reactions are still visible

LOS ANGELES DERMATOLOGICAL SOCIETY

THOMAS W NISBETH, M D, *Secretary*

Jan 14, 1936

NELSON PAUL ANDERSON, M D, *Chairman*

A CASE FOR DIAGNOSIS Presented by DR H P JACOBSON

R K, a woman aged 44, a Hungarian housewife, states that when she was 2½ years old she was burned extensively by hot water The burns healed, leaving a small red area on the right ear and at the left angle of the mouth At that time an area of erythema appeared on the posterior aspect of the left thigh The lesion on the face disappeared, but that on the leg has been growing slowly About four years ago the lesion on the ear began to enlarge after the patient had a serious cold

On the lower half of the right ear there is a lesion which extends forward about 1 inch (2.5 cm). There are also a palm-sized area of erythema on the posterior aspect of the left thigh and a white scar 3 cm in length at the left angle of the mouth. A Wassermann test made on Feb 5, 1935, gave a 4 plus reaction. There is no history of a primary lesion.

Treatment since February 5 has consisted of ten injections of 0.13 Gm of bismuth subsalicylate, ten injections of 3 Gm of neoarsphenamine and three injections of 0.13 Gm of bismuth subsalicylate. The patient has also received applications of ammoniated mercury ointment and cod liver oil and malt extract internally.

No acid-fast organisms were found in a smear made on Feb 13, 1935, a culture also gave negative results. A biopsy made on Feb 9, 1935, showed lupus vulgaris. According to another report (Feb 25, 1935) the changes were more like those of tuberculosis of the skin than like those of syphilis.

DISCUSSION

DR SAMUEL AYRES JR. I think that this disorder is an interesting example of the tumid variety of lupus erythematosus, although it possesses features of lupus vulgaris. Possibly it belongs in the category of disorders exhibiting characteristics which make it difficult to differentiate between lupus erythematosus and lupus vulgaris.

DR SAUL S. ROBINSON. I agree with the diagnosis of lupus vulgaris.

DR L. F. X. WILHELM. The fact that the lesion has been present for forty-four years rules out syphilis. I agree with the diagnosis of tuberculosis.

DR H. S. CAMPBELL. I agree with the diagnosis of lupus vulgaris.

DR H. P. JACOBSON. I know little about this case. I saw the patient for the first time about three months ago at a meeting at which she was presented with the diagnosis of malignant degeneration of the skin. After that I did not see her for three months, then she again came to the clinic, presenting an eruption involving the right ear and the left thigh, the characteristics of which were essentially similar to those now present. Without having had an opportunity to study the slides microscopically I present the patient with a clinical diagnosis of lupus vulgaris of the left thigh and sarcoid of the right ear.

ROSACEA-LIKE TUBERCULID OF LEWANDOWSKY Presented by DR SAUL S. ROBINSON

R. M., a woman aged 25, whose family history discloses no evidence of tuberculosis has an eruption on the face which appeared suddenly six months ago. On the cheeks and chin are areas of closely set papules from the size of a pinhead to that of a millet seed on an erythematous base. A few pustules and scaling papules are interspersed. Examination with the diascopé reveals apple jelly pigmentation in many papules. The patient states that a biopsy made by Dr S. W. Becker, of the University of Chicago, several months ago showed rosacea-like tuberculid of Lewandowsky. The patient states that she received ten injections (gold preparation?) in Chicago and that some clearing of the eruption followed that treatment.

DISCUSSION

DR L. F. X. WILHELM. I think this is an interesting disorder. So far as I recall, it is the first time I have seen this particular type of tuberculosis. According to the history the microscopic picture has definitely shown tuberculosis of the skin.

DR H. S. CAMPBELL. I think the clinical picture is absolutely typical of what it represents. The disorder is rather rare. In approximately two years at the Hôpital Saint Louis, in a well attended outdoor clinic held daily in a community where tuberculids were of comparatively common occurrence, only six cases of this disorder were observed.

DR MOSES SCHOLTZ. I should call this disorder an acne-like but not a rosacea-like tuberculid. There is no telangiectasia. The skin is dry. If any-

thing can be compared with this condition it is a necrotic acne I think that the term rosacea-like is used entirely too loosely

DR KENDAL FROST It seems to me rather important to keep to the terminology when a name such as rosacea-like tuberculid of Lewandowsky is given to the condition It has certain morphologic and prognostic significance

DR SAUL S ROBINSON So far as I know this is the first case of rosacea-like tuberculid of Lewandowsky presented before this society The first cases in this country were recorded by McKee, Sulzberger and Wile This condition has been recognized in Europe since 1917, but only during the past few years have a few cases been observed in this country In lupus miliaris faciei the lesions are deeper, no pustules occur and no erythema or violaceous hue, as exhibited by this patient, is present The histologic picture of rosacea-like tuberculid shows no caseation as does that of lupus miliaris faciei

ARSENICAL DERMATITIS LASTING SIX MONTHS Presented by DR IRVING R BANCROFT

I M, a man aged 22, a Mexican, says that his father had syphilis He exhibits phthisis bulbi, left nystagmus and some atrophy of the optic nerve From July 1934 to July 1935 he received thirty-four injections of an arsenical preparation The administration of arsenic was discontinued in August 1935, when the rash first appeared Sixty-four injections of a bismuth preparation have been given since then, the treatment being continued up to last week The general appearance is good There are numerous oval dry and scaly erythematous itching patches on the body, and on the anterior aspect of both forearms there is a diffuse, sharply margined moist bright red itching rash This rash has not changed much in the last few months Seven Wassermann tests have been made, the reactions have been mostly 1 or 2 plus Scrapings from lesions were negative for mycelia Culture also gave negative results

DISCUSSION

DR H P JACOBSON This is a type of disorder which, I am sure, no dermatologist is eager to treat, as its response to therapy is at best rather slow I am now treating a female patient who presents an eruption closely similar in character to that exhibited by Dr Bancroft's patient Her lesions consist of oval or circular plaques, sharply margined and elevated, resembling for the most part a seborrheic dermatitis but now and then closely simulating pityriasis rosea Some of the lesions may also be mistaken for tinea I am of the opinion that the eruption is a result of bismuth rather than of arsenic medication It is probably a manifestation of allergy engendered by an altered cutaneous reaction to a combined bismoprotein factor The prognosis, as already indicated, is a slow response to therapy, but, on the whole, it is much more hopeful than in the diffuse erythematous squamous type of reaction engendered by arsenic

DR H C L LINDSAY I was impressed by the great resemblance between this type of dermatitis and mycosis fungoides

DR SAMUEL AYRES JR I am rather inclined to believe that the picture is due to the bismuth medication, although that cannot be proved My co-workers and I recently had a patient in whom an eruption appeared on the hands and feet and on some parts of the body during treatment with bismuth only, we regarded the disorder as being due to bismuth I think that this is one argument against concomitant administration of bismuth and arsenic I think that any eruption appearing in the course of anti-syphilitic treatment calls for the discontinuance of all treatment, at least temporarily The configuration of these lesions is interesting They are oval and follow the lines of cleavage of the skin like pityriasis rosea

DR MOSES SCHOLTZ I think that the diagnosis of eruption due to a drug is accepted too easily The fact that a patient has been taking bismuth is no proof that an eruption exhibited by that patient is due to the drug In this case the patches are entirely too well defined to be of medicinal origin, and the mere

fact that the rash spreads when administration of arsenic is continued does not prove that it is due to arsenic. It might be an acute psoriasis which is aggravated by arsenic. Only few eruptions due to bismuth are seen in this country. A rash due to a drug should be more diffuse than that exhibited by this patient, and it would be associated with some other signs of intolerance to the drug. I should not accept this diagnosis until it is proved more conclusively. The disorder may just as well be a mycotic infection.

DR C R HALLORAN The picture is that which is frequently seen in eczema. Irrespective of whether the drug administered was bismuth or arsphenamine, the causative agent in these disorders is arsenic.

DR STANLEY CHAMBERS I agree with Dr Jacobson regarding the fact that the disorder is due to bismuth. The follicular character of the lesions and the pityriasis rosea-like configuration are consistent with this diagnosis. The patient has received an equal number of injections of a bismuth preparation and of arsphenamine.

DR IRVING R BANCROFT I thought that the dermatitis was due to arsenic, and I discontinued administration of the drug. Administration of bismuth was continued until recently. It is my opinion that the disorder was originally due to arsenic medication, that the bismuth therapy kept it active and that the latter should be discontinued while the eruption is as severe as it is at present.

CARCINOMA OF THE BREAST Presented by DR MOSES SCHOLTZ

R R, a woman aged 71, has had high blood pressure. Five years ago she underwent an operation for the removal of the gallbladder and of gallstones. The menopause occurred about twenty years ago. A sore and breaking out at the nipple of the left breast appeared three years ago. This cleared up under treatment at the White Memorial Hospital, where the patient was treated with radiation. Finally she was advised to have the breast amputated—which she refused. Roentgenograms of the chest on Oct 11, 1935, showed solid diffuse shadows, suggesting metastases to both lungs. The patient is a heavy woman. The entire left breast is infiltrated, it measures 6 by 7 cm and is ulcerated in spots. The axillary gland is not palpable. After the cauterized surface healed, peculiar superficial, dark red, slightly scaly, in places moist, irregularly shaped patches appeared on the involved breast. The heart is enlarged toward the right. The blood pressure is 190 systolic and 90 diastolic. Urinalysis showed no albumin, the reaction for sugar was 4 plus. The sugar content of the blood was 138 mg per hundred cubic centimeters. Treatment has consisted of the Percy cautery and intensive roentgen radiation to the right axilla.

DISCUSSION

DR SAMUEL AYRES JR I believe that the disorder is a carcinomatous manifestation. Whether it is a true Paget's disease I do not know.

DR H P JACOBSON I see nothing mysterious about the cutaneous lesion that this patient presents. She is suffering from Paget's disease of the left breast, which, as is well known, is an intra-epithelial or intra-epidermal malignant process. The lesion may have its origin in the epidermal layers of the cutaneous covering or in the milk ducts. In either event the process eventually becomes deep seated, involving the glandular substance of the breast as well as the cutaneous covering of that organ. One of the characteristic cutaneous manifestations in this type of cancer is the eczematoid stage of the skin of the breast, and that is exactly what this patient presents—a sharply margined infiltrated eczematoid eruption of the skin of the involved breast.

DR KENDAL FROST I have seen one or two instances in which the cancer involved the skin, exhibiting flame-shaped infiltrations radiating from the primary source or the operative scar, a condition which I regard as a form of cancer en cuirasse.

DR H P JACOBSON In reply to Dr Frost's remarks I wish to say that cancer en cuirasse is a definite clinical entity. It consists of an extension of a

malignant focus to the surrounding cutaneous covering. The eruption consists of numerous indurated, solid nodules of various sizes and shapes, discrete for the most part but sometimes confluent, and of an associated infiltration and discoloration of the intervening skin, the color varying from bright to dark red. This patient presents no such manifestations, but she does have a characteristic sharply margined and somewhat crusted eczematoid eruption, which is a manifestation of Paget's disease.

DR L. F. X. WILHELM: I regard the disorder as an early stage of Paget's disease of the breast associated with malignant degeneration. Sections from these patches should be taken for microscopic study.

DR MOSES SCHOLTZ: The diagnosis of Paget's disease is correct except for the fact that it is made four months too late. The nipple was destroyed a long time ago. These cutaneous lesions have developed within the last month or two. There is no trace of the nipple left. I am at a loss to account for the lesions. They are superficial and are not associated with induration. They are developing rapidly and are scattered around. A month ago there was only one patch, and now there are four or five. There is a diffuse infiltration of the skin of the chest. As the patient refused radical operation I used the Percy cautery.

EPITHELIOMA Presented by DR IRVING R. BANCROFT

D., a man aged 59, a cigar dealer, states that he had a chancroid twenty-five years ago. Four or five years ago he noticed a red spot on the face. No treatment was given until June 1935, when, after a Wassermann test gave positive results, antisyphilitic treatment was instituted. The lesion was cauterized two months ago. No improvement occurred. Six roentgen treatments consisting of exposures of fifteen minutes each were given. The last treatment was given two weeks ago. The lesion consists of an ulcer and a crusting fungous growth the size of a 50 cent piece. There is no pain or discomfort. The gland in the neck is enlarged. The microscopic diagnosis was epithelioma of the third grade.

DISCUSSION

DR H. P. JACOBSON: This case is instructive and illustrates the necessity of revising some of the technic in the handling of malignant cutaneous degeneration. I also wish to emphasize the necessity of adequacy when treating cancer in any form. Regardless of what method of treatment one may employ in the handling of malignant lesions, the principal consideration must be adequacy of technic. This patient was treated with electrosurgery, roentgen and radium radiation, etc., but none of these methods seems to have been employed with sufficient adequacy to have brought about destruction of the malignant process. He now presents an extensive carcinomatous involvement which if neglected much longer will result disastrously. I also wish to call attention to the fact that infiltration anesthesia was employed by the attending physician in the electrosurgical procedure. I condemn the use of infiltration anesthesia in the management of malignant cutaneous degeneration. In my opinion, the method of choice in handling such disorders is actual cautery, especially in the present case, if an anesthetic should become necessary general anesthesia in one form or another should be employed.

DR SAMUEL AYRES JR: Why does Dr Jacobson object to infiltration anesthesia? If the infiltration is made widely and deeply without striking any cancerous tissue, I fail to see how any damage can occur. The removal by cautery is certainly a fine method of treatment, but it is not the only treatment, and it may not even be the treatment of choice. I should use the endotherm knife and heavily cauterize the base and sides. I fail to see why that method is not applicable.

DR CHARLES R. CASKFY: I cannot agree with Dr Jacobson's ideas about anesthesia. In private practice one has to treat many patients with several

epitheliomas I am afraid the majority of them could not be treated without an anesthetic I do not think that the infiltration spreads the cancer

DR IRVING R BANCROFT The only question in this case concerns the form of treatment The patient has had syphilis, and syphilitic treatment, cautery and roentgen irradiation—the last treatment being given about two weeks ago—have been used The biopsy shows third grade epithelioma I think that any kind of irradiation is definitely contraindicated because of previous treatment of that type I think that the only thing to do is to use a cautery and that the procedure should be carried out by some one who is not afraid to spoil the patient's face

HERPES ZOSTER Presented by DR SAMUEL AYRES JR

This Negress states that her present illness is of three weeks' duration It developed while she was receiving neoarsphenamine for syphilis Slight itching and burning are present The eruption involves the flexor aspect of the fourth finger of the right hand and extends across the palm onto the wrist and up the medial aspect of the forearm half-way up to the elbow The lesions occur as discrete and grouped vesicles, the group is not larger than a navy bean, and the vesicles are small

DISCUSSION

DR IRVING R BANCROFT The patient states that the only way she can stop the itching and burning is to prick the vesicles and let the fluid out I think that the disorder is herpes zoster

DR. H C L LINDSAY The disorder resembles lichen planus This patient has received a certain amount of arsenic, and arsenic produces lesions that resemble lichen planus

DR C R HALLORAN The lesions are lichenoid and deeply pigmented The diagnosis of lichenoid type of eruption should be considered I cannot discern the features of herpes zoster

DR L F X WILHELM Last Monday I saw the patient in a good light There were definite groups of vesicles While I considered the diagnosis of linear lichen planus, I favored that of herpes zoster

DR. SAMUEL AYRES JR The points brought out here are exactly the ones my co-workers and I considered when we first saw the patient I am still not convinced that the diagnosis of herpes zoster is correct The patches themselves are small, and the eruption has the appearance of an annular lichen planus The disorder is interesting

DR STANLEY CHAMBERS My co-workers and I have observed the same picture in a male patient, and we considered the diagnosis of herpes zoster and that of lichen planus The histologic picture was that of a lichen planus

DR. KENDAL FROST I was impressed by the resemblance of those lesions to lichen planus annularis linearis

LOCALIZED MYXEDEMA OF THE LEGS Presented by DR SAMUEL AYRES JR

H I, a man aged 47, underwent partial thyroidectomy for exophthalmic goiter four years ago Lesions appeared on the legs about one year after the thyroidectomy was performed and have not disappeared Exophthalmos is present The eruption is limited to all aspects of the lower portion of the legs, the greatest involvement anteriorly extending two thirds of the way to the knee on the left and half-way to the knee on the right The eruption consists of numerous discrete and almost confluent slightly pinkish, marble-like doughy nodules with a slightly verrucous feel which consist of tiny flat warty structures There is no pitting edema When the skin is stretched the orifices are seen to be considerably dilated The tonsils are large and cryptic Transillumination of the frontal sinuses showed dullness The antrums, especially the right, were dark Transillumination of the gums gave negative results Before operation, four years ago, the basal metabolic rate was +51 per cent On Sept 4, 1933 it was +34 per cent No treatment has yet been given for the cutaneous condition

DISCUSSION

DR W H GOECKERMAN I have seen about half a dozen proved cases of localized myxedema, but I must say that so far as the clinical picture is concerned, that presented by this patient is definitely different from any I have seen. The number of the lesions, the distribution and the purplish hue are different. The ordinary type of localized myxedema is described as being pigskin-like in appearance, and that, I think, is a good description. This patient's lesions do not have that appearance. Yet after a careful consideration of the differential diagnosis, the only diagnosis I can make, chiefly on the basis of exclusion, is localized myxedema. However, the disorder presents a clinical picture definitely different from the manifestations I have seen previously. A careful histologic study should clinch the diagnosis if it is correct.

DR MOSES SCHOLTZ The disorder impressed me as being rather a paradoxical phenomenon. Maybe it is myxedema. On the other hand, I should like to have an explanation, considering the fact that the patient exhibits signs of hyperthyroidism, extreme exophthalmos and sweating.

DR KENDAL FROST Dr Scholtz' remarks are interesting in view of the fact that at the last examination the patient's metabolic rate was $+34$ per cent.

DR STANLEY CHAMBERS I agree with the diagnosis.

DR SAMUEL AYRES JR This is the first case of this condition I have ever seen. The combination of exophthalmos and a high basal metabolic rate together with localized myxedematous changes seems contradictory. The cutaneous lesions appeared six months after the patient underwent an operation for exophthalmic goiter. Two types of lesions have been described—nodular and plaque-like. I think that this is an intermediate disorder, some of the lesions are nodular, some appear in plaques. The question of therapy is a serious one. Some disorders of this type resist all forms of therapy. A few good results have been reported from the use of iodine and thyroid together. Apparently the normal secretion of thyroid is almost lacking in patients with this disorder. At the same time there is a toxic secretion of the thyroid which produces exophthalmos and a high basal metabolic rate. It is rather confusing to see all these manifestations in the same patient.

DR W H GOECKERMAN All observers agree that histologically, tinctorially and histochemically the changes in the tissues are not the same as those of a true myxedema. The name is simply a term applied to lesions of this type in this country which has become popular. There are other terms more descriptive. "Myxedema" is really a misnomer. Dr Ayres' brief dissertation describes the usual course of events in cases of this disorder.

MANHATTAN DERMATOLOGIC SOCIETY

MIHRAN B PAROUNAGIAN, M D, *Secretary*

Jan 14, 1936

PAUL E BECHET, M D, *Chairman*

A CASE FOR DIAGNOSIS (ERYTHROPLASIA?) Presented by DR GEORGE C ANDREWS

E F, a man aged 37, states that about seven months ago he noticed slight itching in the coronal sulcus. For two or three months the irritation would flare up and then regress. Last fall the patient observed two macular areas, one on each side of the frenum. These enlarged peripherally. Urologists considered

the disorder to be a chronic balanitis resulting from incomplete circumcision. Circumcision was performed again one and one-half months ago, after that the lesions joined in the midline to form one sharply outlined red macular area. There was no induration. Apparently the lesion healed at times as a result of application of bland ointments and then recurred. There was no scaling until one month ago. The Wassermann and the Kahn test were negative. The patient has taken about one tablet of allylisopropyl barbituric acid and aminopyrine every three weeks during the past few months.

Microscopic examination showed thickening of the epidermis due to acanthosis. There was no dyskeratosis. The interpapillary areas contained some hydropic cells. In the cutis there was a congestion of the blood vessels, and moderate perivascular cellular infiltration was observed.

DISCUSSION

DR GEORGE M. MACKEE It is always difficult to make an unequivocal diagnosis in cases of this disorder because at present a complete composite clinical and histologic concept of erythroplasia is lacking. In most cases there is free exudation, in this case no exudation has been present, but perhaps there is a dry type of erythroplasia. Erythroplasia is supposed to be always sharply margined. This patient's lesion is well margined except at one point. There are a number of papular satellite lesions, which are not supposed to occur in erythroplasia but which, however, may prove to be a part of the picture after more is known about the disease. Erythroplasia, like Paget's disease, is not supposed to improve spontaneously, that is, it shows no remissions and exacerbations. According to the patient's statement this lesion has shown improvement at times. Perhaps his statement is not reliable. It is possible also that it will later be discovered that erythroplasia may improve at times and that to some degree improvement may be spontaneous. The histologic picture is not that of erythroplasia, but perhaps a second biopsy will show an entirely different picture. At present I cannot subscribe to the diagnosis of erythroplasia, but certainly that possibility should be kept in mind. I am more inclined to consider a diagnosis of a fixed eruption due to a drug or of psoriasis.

DR LUDWIG OULMANN I should not consider the diagnosis of erythroplasia. In erythroplasia there is a fairly smooth surface and the process goes deeper, while the clinical picture in this case is a papillary structure due to dyskeratosis.

DR ANDREW J. GILMOUR I have nothing to add. My impression is that the disorder is psoriasis.

DR ISADORE ROSEN It is difficult to make a diagnosis after one examination of a disorder like this. On clinical grounds alone I should be inclined to agree with the members who believe that the condition is psoriasis. Psoriasis when it occurs on the glans penis does not as a rule show the same features as when it affects the trunk or other parts of the body. One of the reasons for the difficulty in making a diagnosis is the fact that the patient has received a great deal of treatment.

DR J. FRANK FRASER I can see no evidence of malignant degeneration in the section. The histologic picture suggests psoriasis.

DR FRED WISE I agree with the opinions expressed by Dr. MacKee. I believe that if the lesion were left alone for a week or two it would more nearly resemble psoriasis. It is quite possible that the whole histologic picture would change on an untreated area.

DR GEORGE C. ANDREWS The patient has consented to undergo another biopsy. The lesion did disappear, but that was after it was excised by the operation for circumcision. The patient says that the lesion has always been dry, but I have seen it when it was fairly moist. I shall follow Dr. Wise's advice and let it alone for a while and then make a biopsy.

A CASE FOR DIAGNOSIS (DUHRING'S DISEASE?) Presented by DR PAUL E BECHET

E. M., a woman aged 46, a housewife, born in the United States, who is under the care of Dr Mihran B Parounagian, states that an eruption developed on the chest about seven weeks ago and later spread to the neck and face. The eruption appeared as large blisters, later reddening of the skin and formation of crusts developed. The patient has not been aware of any lesions in the mouth. There has been some burning of the skin in the affected areas, but there is no itching. The patient states that she has taken no drugs except compound effervescent powders U S P and magnesium citrate.

The lesions are most marked on the anterior aspect of the chest and on the lateral and anterior aspects of the neck. There are scattered lesions on the face, and a few are present on the forearms, left thigh and auricles. The chief elements are bullae and crusted lesions, and considerable surrounding redness and inflammation of the skin are present. There are no lesions on the lips or in the mouth. The patient applied a 3 per cent ammoniated mercury ointment, which brought about only slight improvement, in fact new lesions (bullae) appeared. On January 6 a patch test with potassium iodide on the right forearm showed a strongly positive reaction, consisting of erythema with formation of vesicles. Almost at once after application of potassium iodide ointment the patient noted quite marked itching in the old lesions. The itching is still present. The Wassermann test was negative. The blood cell count showed 4,650,000 red cells, 12,100 white cells and 73 per cent hemoglobin. The results of the differential count were as follows: polymorphonuclear neutrophils, 66 per cent, lymphocytes, 29 per cent, eosinophils, 5 per cent.

DISCUSSION

DR GEORGE M. MACKEE: There is nothing about the eruption which to my mind suggests dermatitis herpetiformis. The striking features are the widespread erythema on the exposed areas of the chest, face and lobes of the ears and the numerous discrete bullae. In the absence of bullae one would consider the possibility of lupus erythematosus. The bullae, of course, suggest pemphigus provided an eruption due to a drug and erythema multiforme can be ruled out. I suggest the Senear-Usher syndrome as a possible diagnosis.

DR ANDREW J. GILMOUR: The eruption may have been affected by the cold weather or by the sun's rays, as it is located mostly on the surface exposed to the elements. I cannot suggest a diagnosis.

DR MAX SCHEER: I think that the eruption is due to exposure to light plus some added sensitizing factor or lupus erythematosus of the bullous type.

DR PAUL E. BECHET: Dr MacKee's suggestion is excellent. The eruption affects exposed parts of the body and there is a sharp line of demarcation, these features suggest the possibility that actinic light was an etiologic factor.

A CASE FOR DIAGNOSIS (PSORIASIS? MYCOSIS FUNGOIDES?) Presented by DR FRED WISE

Mrs F. V., a woman aged 50, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, presented herself for treatment on Oct 28, 1935, because of an eruption of about two months' duration. About fifteen years ago a scaly eruption appeared on the knees and elbows, remaining confined to these areas. This eruption subsided but reappeared in the same locations seven years ago and again two years ago, the last eruption has persisted to the present time. At present there is a widespread dermatitis involving the knees, elbows, trunk and scalp. On the upper and lower extremities, especially in the regions of the knees and elbows, are large scaly and crusted patches resembling psoriasis. On the trunk are widespread pink diffuse scaling areas in the midst of which are islands of uninvolved skin in the shape of irregular discoid formations. On the chest and back are scattered patches of infiltrated skin from 1 to 4 inches (2.5 to 10 cm) in diameter which are slightly elevated, dark red

and somewhat scaly, resembling early lesions of mycosis fungoides. The lower portions of the ear lobes present a glistening, indurated and thickened dermatitis. The scalp is covered with adherent scales, the involvement being most pronounced anteriorly. The finger-nails are striated longitudinally but not pitted. Superimposed on these chronic lesions there is evidence of an acute diffuse follicular and scaly dermatitis evidently due to the recent use of some irritating topical remedies. The patient complains of intolerable itching and exhibits many marks of scratching. The Wassermann and Kahn tests were negative. The results of histologic examination will be reported at a subsequent meeting.

DISCUSSION

DR MAX SCHEER I think that the disease is mycosis fungoides. On the back there is an oval infiltrated lesion which resembles mycosis fungoides. Other lesions have changed as a result of treatment.

DR ANDREW J GILMOUR I could not see any evidence of psoriasis, but I think that the diagnosis of mycosis fungoides is correct.

DR ISADORE ROSEN There is no question but that this patient has some lesions not unlike psoriasis, but there are also lesions scattered over the trunk which have features strongly suggestive of mycosis fungoides. Further studies and repeated histologic examinations will have to be made before a definite diagnosis can be arrived at.

DR J FRANK FRASER I am inclined to favor the diagnosis of mycosis fungoides. There is a history of intense itching, and the clinical picture suggests the *honnme rouge* type of that disease. Experience leads me to believe that a mutation from psoriasis to mycosis fungoides does not occur. In a patient who is still under observation the earliest clinical picture closely resembled that of psoriasis, and several members of this society subscribed to that diagnosis. Several biopsies were made, and the histologic picture supported the clinical diagnosis of psoriasis. Later when tumors developed and the microscopic picture became typical of mycosis fungoides a study was made of the sections obtained in an early stage of the disease on which the diagnosis of psoriasis had been based. In one field of one of these sections the typical reticulo-endothelial reaction with mitotic figures showed that the early clinical and histologic diagnoses were incorrect. The condition was mycosis fungoides all the time.

DR GEORGE M MACKEE I doubt that there is ever a transformation of psoriasis into mycosis fungoides. It is well known that the prefungoid stages of granuloma fungoides may for months and years so closely resemble other diseases, such as parapsoriasis, psoriasis and different clinical varieties of eczema, that for long periods it is impossible to make the differentiation either clinically or histologically. The repeated discussions relative to this question can be applied to many dermatoses that at times closely simulate one another, namely, syphilis, tuberculosis, eczema, psoriasis, etc. As a matter of fact, clinical entities rest on rather insecure grounds. Often, indeed, their identities may be questioned. Dr Wise's patient presents some lesions that suggest psoriasis, some that suggest mycosis fungoides and some that suggest eczema. For instance, the eruption on the knees resembles the variety of eczema known as neurodermatitis circumscripta, which is often difficult to differentiate clinically from psoriasis. It is possible, of course, for a patient to have more than one disease. It is possible that this patient has mycosis fungoides. If that is the case I believe that the disorder was mycosis fungoides from the beginning, I do not think that a change from psoriasis or eczema to mycosis fungoides has occurred.

DR PAUL E BECHET The lesions on the knees are almost typical of neurodermatitis. There is a patch on the back which is sharply outlined and somewhat infiltrated. The diagnosis of mycosis fungoides should be considered. Dr Fox reported one or two cases of psoriasis in which the manifestations remained typical of that disease for fifteen or twenty years and then developed into those of mycosis fungoides. I do not believe that a transition from psoriasis into

mycosis fungoides does occur. These disorders, though resembling psoriasis, are primarily atypical mycosis fungoides. In my opinion it is possible for mycosis fungoides to exist for many years without going on to tumor formation and to fatal termination, and in its early stages it frequently assumes the appearance of eczema or psoriasis with such success as to confuse the most astute observer.

DR HOWARD FOX The case to which Dr. Bechet referred was one which I reported. It was that of a man who for twenty-eight years had suffered from what appeared to be ordinary psoriasis and whose condition had been diagnosed as such by numerous dermatologists. When I saw him the eruption had changed and a clinical diagnosis of the infiltrative stage of mycosis fungoides was made. This was confirmed by histologic examination.

DR FRED WISE In this case one should be guarded in making the diagnosis of psoriasis, mycosis fungoides or a combination of both diseases. A histologic report will be submitted at a later date.

NOTE—A subsequent microscopic examination revealed mycosis fungoides.

RECKLINGHAUSEN'S DISEASE Presented by DR. PAUL E. BECHET

L. N., aged 23, presented herself at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Nov. 30, 1935, with an eruption of one year's duration. There are scattered lesions over the abdomen and back and isolated lesions on the arms. The lesions are pea-sized, elevated, soft and violaceous tumors. Digital compression causes them to disappear through a ring in the skin; release of the pressure causes a return to the normal elevated position. The patient presents no café au lait spots. The Wassermann and Kahn tests were negative. Urinalysis gave normal results. A biopsy of material from a lesion on the right arm revealed a microscopic picture typical of Recklinghausen's disease.

DISCUSSION

DR. FRED WISE An interesting feature is the fact that the father of the patient had a number of café au lait spots on the body but no other lesions of Recklinghausen's disease.

SEBORRHEIC DERMATITIS AND FOLLICULITIS Presented by DR. PAUL E. BECHET

A. O., a woman aged 22, presented herself at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Jan. 14, 1936, with an eruption involving the scalp, face, ears, axillae, region beneath the left breast, umbilicus, pubic area and groins. The eruption consists of numerous discrete and confluent erythematous patches, some of which are sharply margined while others fade into normal skin. These patches are oozing. The lesions on the scalp are covered with an adherent greasy grayish white scale. The results of examination for tinea made today have not been reported. The patient was hospitalized at the Bellevue Hospital for one and a half months, at the Metropolitan Hospital for eleven months, at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital for two months and at the New York City Hospital for one day. The patient states that she has a moderate vaginal discharge.

DISCUSSION

DR. FRED WISE The only therapeutic suggestion I can offer is to paint the lesions with a 2 per cent solution of gentian violet.

DR. GEORGE M. MACKEE Years ago I should have unhesitatingly made a diagnosis of seborrheic eczema. Now I am more careful. The inclination is to make the diagnosis of seborrheic eczema for the basic trouble complicated by the secondary variety of eczema known as infectious eczematoid dermatitis. However, I agree with Dr. Rosen that the diagnosis of moniliasis and that of the exudative type of psoriasis must be considered.

DR PAUL E. BECHET This condition is found as often in males as in females, thus somehow tends to decrease the importance of vaginal organisms as a causative factor. My impression of this disorder is that the eruption begins as a typical seborrheic dermatitis in locations generally affected by seborrhea—the scalp, face, chest, axillae, umbilical and genital region—and that a secondary staphylococcal due to infection or lowered resistance on the part of the patient supervenes, the disorder thereby resulting in the typical weeping pustular dermatitis so commonly observed. This type of disorder is extremely resistant to treatment, and in dermatologic departments of hospitals there are always at least one or two patients with that condition. At rare intervals a plan of treatment almost effects a cure in a patient, and yet the same therapy has no effect whatever on another patient with a similar disorder.

A CASE FOR DIAGNOSIS (TOXIC MELANODERMA?) Presented by DR MAX SCHEER

J. Y., a woman aged 27, presented herself at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Dec 14, 1935, because of an eruption of thirteen years' duration. It was not accompanied by any subjective symptoms, and the patient applied for treatment only because she feared that other areas would become involved. The eruption is confined to the middle portion of the anterior aspect of the chest and to the back as far down as the lower part of the lumbar region. The primary lesion was a pinhead-sized pigmented macule which varied in color from light brown to dark brown. Pigmented spots of this kind dot the entire affected area and give it a mottled appearance. The skin between the spots is normal. Wassermann and Kalin tests were negative. The report on the histologic examination stated that the disorder fits in with the picture of toxic melanoderma as described by Riehl.

DISCUSSION

DR MAX SCHEER I do not believe that the disorder is Riehl's melanosis. There is no history of a dietary deficiency. Moreover, there are lesions on the covered parts of the body, a feature which is not found in Riehl's melanosis.

ERYTHEMA INDURATUM Presented by DR FRED WISE,

Mrs. J. O., aged 19, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, presents an eruption on the lower aspect of both legs, the disorder is of three years' duration. On the lateral aspects of the right leg above the ankle and on the posterior aspect of the lower portion of the left leg the eruption consists of erythematous and violaceous roughly oval plaques with well defined borders. The skin appears to be glazed, slightly indurated and somewhat edematous. In the course of her work the patient frequently enters a butcher's icebox. The noteworthy feature because of which she is presented is the fact that tuberculin tests on Jan 4, 1936, were negative with dilutions of 1 10,000, 1 100,000 and 1 1,000,000. Roentgenograms of the chest made on Jan 11, 1936, showed no abnormalities.

DISCUSSION

DR GEORGE M. MACKEE I think that the disorder is typical Bazin's disease clinically. Histologically it may prove to be one of the closely allied conditions, such as so-called perivasculitis or periphlebitis nodularis.

LUPUS VULGARIS Presented by DR ISADORE ROSEN

S. R., a man aged 34, presented himself at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital for treatment of an almond-sized erythematous infiltrated area on the lateral margin of the sole of the left foot of about fifteen years' duration. A biopsy made on Jan 6, 1936,

showed typical lupus vulgaris. The patient also presents some scaling of the palms and soles. The culture was negative for the organism of tinea. The Wassermann and Kahn tests were negative.

RECURRENT RASH OF SECONDARY SYPHILIS Presented by DR ISADORE ROSEN

H. H., aged 26, presented himself for treatment at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. The patient was exposed to infection in the last week of August 1935, and a lesion appeared on the glans penis on Sept. 10, 1935. He applied iodine locally for one week, then he went to a physician, who treated the lesion locally for a week and then made a blood test, the result of which was 4 plus. No dark field examination was made. There was swelling of the left inguinal glands. The patient was referred to a clinic, where he was found to have a roseola. He had no headache, sore throat, fever or pains in the joints. He was given one injection of arsphenamine at that clinic and was then referred to the Board of Health for further treatment. There he received twelve intravenous injections of arsphenamine followed by four intramuscular injections of a bismuth preparation. He then failed to present himself for treatment for one month. When he returned he received two more injections of arsphenamine, and thereafter he was treated at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. The roseola disappeared after the fourth injection of arsphenamine. The present eruption appeared immediately after the eighth injection of the first course, and the left arm became painful and swollen, remaining so for a week, a few days after the onset of the swelling the present itchy rash appeared on the whole body, it has persisted unchanged for the past seven weeks. Treatment was continued but had no influence on the rash.

DISCUSSION

DR FRED WISE. My diagnosis of the cutaneous eruption is syphilis.

DR MAX SCHEER. I think that the lesions are psoriasis. It might be worth while to try the *grattage methodique* advocated by Brocq.

DR GEORGE M. MACKEE. In places the eruption suggests psoriasis, in other places it suggests syphilis. Configuration occurs in both conditions. The color in this case is more in favor of syphilis. The main point, however, is that the crusts represent ulceration and not the accumulation of scales so typical of psoriasis. Cases of this disorder were common years ago. The patient requires a continuation of antisiphilic treatment judiciously administered, but he also needs building up and, perhaps, some fever therapy.

A CASE FOR DIAGNOSIS (SYPHILIS? PEMPHIGUS?) Presented by DR ISADORE ROSEN

A. I., a man aged 35, was born in Turkey. He has been married for eight years and has three children, the youngest of which is 14 months old. On admission he stated that he had a gonorrheal infection seventeen years ago. About five months ago, after he was exposed to infection, a lesion developed on the shaft of the penis. At that time his physician found that he had a positive Wassermann reaction and gave him five injections of arsphenamine—the dose was not stated—and five injections of a bismuth preparation. The patient presents an eruption on the forehead, face, chest, back, arms and legs. There are various types of lesions. On the forehead and face there are papular scaling lesions strongly suggestive of syphilis. On the chest and back the lesions are raised, being covered with heaped-up scales, and resemble either a rupioid syphiloderm or psoriasis ostreacea. Interspersed are grouped papulosquamous lesions which suggest secondary syphilis. On the arms and legs the lesions closely simulate psoriasis, although the elbows and knees are not involved. On the glans penis there are annular lesions, raised above the level of the skin, covered with a translucent scale and resembling those seen in keratosis blennorrhagica. There

is no generalized adenopathy, and repeated examinations from smears of the lesions failed to demonstrate spirochetes. The Wassermann test has been repeatedly negative. Biopsy showed a marked round cell infiltration around the blood vessels. The character of the inflammatory exudate in the corium was considered suggestive of syphilis. The patient has received arsphenamine and a bismuth preparation, but despite this therapy new lesions have appeared, and the older ones have not been influenced to any great extent.

DISCUSSION

DR FRED WISE I believe that the patient has pemphigus.

DR GEORGE M. MACKEE I think that the eruption is a syphilitic for the reasons given in the discussion of the similar disorder in the other patient presented by Dr. Rosen.

DR LUDWIG OULMANN I am glad that Dr. Wise made a diagnosis of pemphigus. I asked Dr. Rosen whether he had made a Pels-Macht test. I agree with Dr. Wise.

DR. ANDREW J. GILMOUR My diagnosis is syphilis.

A CASE FOR DIAGNOSIS (GRANULOMA ANNULARE [?] OF THE FACE RESEMBLING EPITHELIOMA) Presented by DR. GEORGE C. ANDREWS

E. O., a man aged 40, is presented because of a lesion which began five years ago as a small papule on the left lower eyelid. He was a boxer at the time and received frequent blows on the eye. The lesion has never been tender. It has been treated with caustic remedies, but it has spread peripherally in spite of this. The patient has a fistula to the right of the anus. On the left lower eyelid there is an oval lesion with serpiginous outline, the periphery of which consists of a pearly ridge. The center is smooth and atrophic and shows some crusting. On the right cheek just below the eye there is a papule the size of a split pea, the consistency and color of which resemble those of the border of the lesion on the left lower eyelid.

NOTE—A subsequent biopsy revealed basal cell epithelioma.

CHICAGO DERMATOLOGICAL SOCIETY

MAX S. WIEN, M.D., *Secretary*

Regular Meeting Jan. 15, 1936

DR. WILLIAM ALLEN PUSEY, *President, Presiding*

ATROPHODERMA WITH TELANGIECTASIA Presented by DR. OLIVER S. ORMSBY

This Polish woman, aged 56, presents a disorder of forty-six years' duration. She was presented before this society in 1928, 1929 and 1930 and before the American Dermatological Association in June 1933. A full description of the clinical symptoms, history and progress together with the results of histologic examinations is given in the ARCHIVES (18:306 [Aug.] 1928, 20:388 [Sept.] 1929, 21:666 [April] 1930, 29:157 [Jan.] 1934).

The changes noted at present from the condition described in the last of the aforementioned references are as follows. On the face the skin shows no activity of the process and practically no sequelae. There are less scaling and less evidence of inflammation, but there is increased telangiectasia over the breasts. Over the anterior and posterior aspects of the trunk and over the arms there is less

scaling, but the wrinkling, atrophy and telangiectasia are unchanged. The ring of superficial pale red flat nodules situated above the knee has extended and developed into a plaque several inches in diameter. Itching continues in this plaque and in scattered areas elsewhere, but it is less severe and is greatly restricted in its distribution. There is no change in the general health.

DISCUSSION

DR PAUL A. O'LEARY, Rochester, Minn. I have seen this patient on several occasions, and I believe that in the differential diagnosis idiopathic atrophy and poikiloderma atrophicans vasculare should be considered. While examining the patient I thought momentarily of the possibility, first called attention to by Dr. Otto Foerster, of the association of mycosis fungoides and poikiloderma. However, I believe that this patient presents an idiopathic atrophy of the skin.

DR OLIVER S. ORMSBY. No new developments have occurred since June 1933, when the patient was presented before the American Dermatological Association. She has been seen by Professor Bloch and Professor Jadassohn and also by a number of the eminent dermatologists in this country, and her condition has not been definitely diagnosed. It is probably not an example of poikiloderma. The pruritus is unusual, and so is the extensive telangiectasia. The histologic picture closely resembles that of idiopathic atrophy. As previous investigation revealed no important findings, the disorder must still be classified as "atrophy-derma with telangiectasia."

ANETODERMA ERYTHEMATODES, JADASSOHN (DERMATITIS ATROPHICANS MACULOSA WITH BALLOONING). Presented by DR. O. H. FOERSTER, Milwaukee, DR. H. R. FOERSTER, Milwaukee, and DR. LESTER M. WIEDER, Milwaukee.

L. J., a boy aged 12 years, is presented because of a cutaneous eruption not associated with systemic symptoms which was first observed in December 1934 and which has steadily increased. The lesions are symmetrically distributed over the upper portion of the chest and back; they do not extend below the transverse nipple line anteriorly or below the lower borders of the scapulae posteriorly and do not involve areas above the jaws and above the hair line. There are a few lesions on the upper extremities, but most of the eruption occurs on the upper portion of the chest and on the posterior aspect of the shoulders.

The lesions are pink to red round or oval macules varying in diameter from 2 mm. to 2 cm., some older lesions exhibit a grayish cast. The smallest and earliest lesions are slightly raised infiltrated red maculopapules showing exaggerated surface markings; the largest are dull pink macules with a wrinkled atrophic surface. Many of the latter lesions exhibit a domelike elevation which is easily invaginated by pressure and "balloons" when pressure is released.

There is an abnormal development of adipose tissue, particularly of the breasts, hips and thighs. The mother states that the boy developed rapidly after the eighth year, putting on an excess of weight—he now weighs 115 pounds (52 Kg.)—and that he exhibited stiffness and physical lethargy at play. There has been a recent disability of the left hip. Mental development is apparently normal.

He has had headache almost daily since childhood, the headache is particularly severe and is associated with vomiting when meals are delayed. Because an endocrine factor, possibly pituitary involvement, was suspected, it was suggested that the patient undergo a complete clinical and laboratory investigation, and he was advised to go to the Mayo Clinic.

The following findings were recorded at the Mayo Clinic. The metabolic rate was -22 per cent, roentgenograms of the chest and skull showed no abnormalities, examination of the urine, a tuberculin test and a serologic test for syphilis gave negative results. Examination of the blood showed 4,350,000 erythrocytes, 11,300 leukocytes and 92 per cent hemoglobin. The results of the differential count were as follows: neutrophils, 65 per cent, eosinophils, 25 per cent.

lymphocytes, 25 per cent, monocytes, 7 per cent. Studies of the chemical composition of the blood were not made. The orthopedic department diagnosed the condition in the hip as "slipped epiphysis." Dr. Montgomery and a pediatrician saw the patient, and Dr. Montgomery suggested the possibility that the cutaneous condition represented multiple benign tumor-like new growths of the Schweninger and Buzzi type or an abortive form of Recklinghausen's disease, after studying sections subsequently submitted to him he expressed the opinion that the histologic picture was consistent with that of the former disease.

The histologic section of an intermediate lesion studied by my co-workers and me showed atrophy of all the layers of the epidermis, condensation and some fragmentation of the collagen, atrophy of the cutaneous glands and narrowing of subpapillary vessels, with moderate infiltration of round endotheloid cells about the vessels. The elastic tissue was absent in the center of the lesion, in other areas it was reduced and fragmented.

DISCUSSION

DR WILLIAM ALLEN PUSEY This condition, I think, belongs in the group of disorders of which I presented the first American example several years ago with the diagnosis of multiple benign tumor-like new growths of the skin of the Schweninger and Buzzi type. In my case I regarded the disorder as a congenital defect in the skin, there was great thinning in the corium, which resulted in ballooning of the subcutaneous tissue through the weak spots in the corium. It is not surprising that other congenital defects of the skin should occur in association with such weak spots.

DR HAMILTON MONTGOMERY, Rochester, Minn. At the Mayo Clinic my co-workers and I have observed a number of cases of Recklinghausen's disease in which varying numbers of lesions have presented the features of ballooning. Histologically this was proved to be due to the destruction of the elastic tissue. I think that Recklinghausen's disease and multiple benign tumor-like new growths of the Schweninger and Buzzi type are closely allied and may even be variants of the same process.

DR RICHARD S. WEISS, St. Louis. Have roentgenograms been made of the skull, particularly with reference to the condition of the frontal bone? Dr. Sherwood Moore described a syndrome under the name of hyperostosis frontalis interna (*Surg., Gynec. & Obst.* 61:345 [Sept.] 1935), this boy seems to present some symptoms that led me to think that he may be suffering from that condition. Headaches and a peculiar type of obesity are associated with the syndrome, and it would be interesting to investigate the patient from this standpoint.

DR OLIVER S. ORMSBY When patients with this condition were first seen they were thought to have Recklinghausen's disease, but I think now that their disorder is considered a disease per se.

DR RUBEN NOMLAND I think that this boy presents symptoms that are usually known as anetoderma erythematodes of Jadassohn. The early atrophic lesions are red, which is usually not the case in macular atrophy. Dr. Ebert recently called attention to the fact that red atrophic striae occur in women who have not been pregnant and even in males. His patients with atrophic striae apparently had an endocrine dysfunction. It is probable that this boy has an analogous syndrome but that the reaction occurred in macules and not in striae.

DR H. R. FOERSTER, Milwaukee. The lesions at their onset are small and definitely infiltrated, but they rapidly become atrophic as they enlarge, and they are inflammatory throughout. There have been no linear lesions and no striae distensae. We believe this condition to be similar to Jadassohn's anetoderma erythematodes, which in his textbook Dr. Ormsby classifies under macular atrophies. In our case we excluded the Schweninger-Buzzi syndrome because of the absence of infiltration and because of the inflammatory character of the fully developed lesions. The lesions in the Schweninger-Buzzi syndrome are described as slate gray and as exhibiting palpable infiltration. We believe that this patient has an

endocrine disorder, possibly involvement of the pituitary gland, and that the cutaneous lesions are only one feature of his disease, which may be Frohlich's syndrome

ONYCHOLYSIS Presented by DR F E SENEAR

This girl, aged 9 years, about one year ago, without having exhibited any preceding inflammatory reaction, shed a toe-nail. The nail regrew and was of normal appearance. Later one finger-nail behaved similarly, and since then the mother has noted discoloration of four finger-nails associated with separation of the plate from the bed.

When the patient was seen in November 1935 the nails of the left great toe and left second toe were yellow and friable. The nails of the ring finger of the right hand and of the two outer fingers of the left hand showed separation from the bed. The plates were smooth, and one of them was of typical egg-shell color.

DISCUSSION

DR H R FOERSTER, Milwaukee. Dr Everett Fox, of Dallas, Texas, has observed a number of cases of separation of nails from the nail bed and loss of nails, in all of which he noted hypothyroidism. Normal growth of the nails is said to have followed the administration of thyroid extract.

DR WILLIAM ALLEN PUSEY. It is interesting to see patients with these disorders, and it is only by studying such disorders that one can hope to get some real information about them. At present there exists a state of confusion regarding all these disorders of the nails.

INOCULATION TUBERCULOSIS WITH SCROFULODERMA Presented by DR S W BECKER

This boy, aged 4 years, noted a "wart" on the right heel three months ago. A little pus could be expressed from the lesion. A few days later red streaks were noted on the leg, and the lesion on the heel was incised by a physician. A swelling was noticed in the femoral region, and the incised wound drained a small amount of pus. On the median side of the right heel was a nonelevated slightly erythematous rough lesion about 1 cm in diameter. In the right femoral region were two swellings of about the same size, one of which was draining purulent material.

Culture of material from the femoral region, which had not yet broken down although it was fluctuant, showed *Staphylococcus albus*. Inoculation of guinea-pigs gave positive results for acid-fast bacilli.

A section removed from the lesion on the heel showed numerous tubercles with large giant cells.

An intradermal test with a 1:100,000 dilution of old tuberculin gave a positive reaction on the right arm.

DISCUSSION

DR HENRY E. MICHELSON, Minneapolis. This patient is presented with a diagnosis of inoculation tuberculosis with scrofuloderma. If one accepts the findings in their component parts I quite agree with the diagnosis, but I should like to consider the lesion on the foot and that on the groin together and call the entire picture a primary tuberculous complex of the skin. I think that the child had an implantation of tubercle bacilli on the foot, and probably he was free from tuberculosis at the time of the implantation. It is of course impossible to know what the reaction to tuberculin was at the time of inoculation. The infection spread by way of the lymphatics, and at the glandular barrier a new reaction was set up, which has erupted through the skin. Even though the child is now examined for tuberculosis with the most scrupulous care, it is possible that a primary pulmonary complex has been present, but it cannot be demonstrated with roentgen rays unless the glands have become calcified. My conception of the primary complex of tuberculosis in the skin is an implantation of infection into the skin of a subject free

from tuberculosis resulting in the development of a lesion at the site of implantation and subsequent involvement of the regional glands

The treatment should be that used for tuberculosis, and locally the lesions may be treated with heat or roentgen rays, and the glands may be treated in a like manner or excised. The tendency of the lesion at the site of inoculation is to heal. Healing of the glandular lesion is much slower. The prognosis, provided reasonable treatment is given, is good.

DR OLIVER S ORMSBY. I presume Dr Michelson refers to the type of lesion which English authors have called a tuberculous chancre and which is now termed a primary complex. My co-workers and I observed such a lesion in a girl about 16 years old who had been seen for other conditions. She presented a lesion simulating a chancre on the brow near the inner canthus and had enlarged glands in the neck. A short time later Professor Bloch saw her. He definitely considered the lesion a primary complex. He brought up the point that the lesion might not be a primary chancre but might be a metastasis from an internal focus. The patient has been under observation for several years, and a roentgenogram of the chest has revealed no signs of tuberculosis. She recovered without exhibiting further lesions, and the primary lesion disappeared as a result of roentgen therapy.

DR PAUL A O'LEARY, Rochester, Minn. Dr Michelson and I have discussed the problem presented by this child on several occasions before the Minnesota Dermatological Society. Our ideas differ on the interpretation of the term primary complex. I prefer the term inoculation tuberculosis for this characteristic tuberculous chancre and bubo to which Stokes called attention ten years ago. The advocates of the term primary complex attach great significance to the presence of a negative reaction to tuberculin before the appearance of the tuberculous chancre, a finding which, I believe, is too variable to be the essential feature in the diagnosis of inoculation tuberculosis. However, I agree that the chancre is a primary infection in a person who does not have tuberculosis and has a good defensive reaction to the disease. I have for several years endeavored to prove that the bovine or the avian type of the tubercle bacillus was the cause of this pathologic entity, but I have not been successful thus far. In my experience when the primary lesion and the bubo have been excised—a procedure which I have followed in the majority of cases which have come under my observation—recurrences or metastases have not occurred.

DR HAMILTON MONTGOMERY, Rochester, Minn. At the Mayo Clinic there recently was a patient, a child, who presented a true primary cutaneous tuberculous complex. She had a mosquito bite on the cheek, this became infected and presented an ecthymatiform appearance, and the adjacent glands in the neck became enlarged. Roentgenograms of the chest showed no evidence of tuberculosis, and the tuberculin test was negative at the time of the initial examination. Two weeks later the tuberculin test was positive, and the gland had broken down. Biopsy revealed a nonspecific type of infiltrate in one area with many bacilli, and adjacent thereto early tubercle formation with epithelioid cells and a few giant cells, in the latter area no tubercle bacilli were present. In this case all the criteria for a primary cutaneous tuberculous complex were present, and I think that if Dr Becker had had the opportunity of examining his patient early enough in the course of the disease he would have found first a negative and later a positive reaction to tuberculin.

In contrast, my co-workers and I have observed other cases of inoculation tuberculosis, generally in older persons, in which we could not be sure whether or not the patients had tuberculosis before the symptoms appeared. In those cases the primary chancre early reveals the specific tubercle formation histologically and shows the apple jelly nodules clinically. This type of lesion is often seen in farmers and veterinarians, possibly it is due to external infection with avian or bovine tuberculosis.

All types of tuberculosis in the fully developed stage reveal specific tubercle formation, both in the primary chancre and in the adjacent glands, and marked caseation necrosis.

DR. S. W. BECKER When this child was first seen the original lesion on the heel had practically healed and there was fluctuation in the femoral node. The patient was on the surgical service and was seen in consultation, and I suggested the possibility of tuberculosis. A few weeks later she was brought back with inflammation in the primary lesion and apparent extension of the process in the groin. When a section for biopsy was taken the whole lesion was cauterized because it was convenient to perform the operation at that time. My co-workers and I are planning to excise the glands, although, as Dr. Michelson stated, there is a possibility of tuberculous infection in the wound.

SCLERODERMA, SCLERODACTYLIA Presented by DR. OLIVER S. ORMSBY

This girl, aged 5 years, presents a disorder of eight months' duration. The first symptom noted was stiffness of the fingers. When this was noted the child was examined, and it was found that the texture of the skin of the forearm felt abnormal and that there was a thickened spot on the chest. Within a month other areas of depigmentation were noticed.

The right arm and right side of the face are somewhat smaller than the left. The last three fingers of the right hand are fixed in flexion, firm to the touch, waxy white and somewhat smaller than normal. There is a definite firmness palpable in the subcutaneous tissues and muscles of the right forearm, and similar changes are found in the external aspect of the right lower extremity. An ivory-colored plaque measuring approximately 2 by 6 cm. involves the entire thickness of the skin of the medial surface of the right biceps. There is a similar plaque measuring 1 by 2 cm. over the sternum, and a somewhat smaller lesion is located over the right temple. An elongated plaque of this type runs beneath the ramus of the right jaw. There is a mottled depigmentation on the right side of the body, it is most noticeable over the medial surface of the right arm and on the right side of the chest and right flank, extending down the right lower extremity. The same type of depigmentation extends across the hips to the left side. A similar change is noticeable about the umbilicus. The remaining skin of the trunk seems to exhibit a slight degree of hyperpigmentation.

DISCUSSION

DR. PAUL A. O'LEARY Rochester, Minn. I had the opportunity to examine this child two weeks ago, and I believe that her disorder belongs in the group of hemiatrophy rather than in that of scleroderma per se. My reason for this distinction is that this condition apparently develops as the result of cerebral injury caused either by infection or by trauma, which in turn produces the sclerodermatous plaques or bands. In several of my cases a cervical and lumbar sympathectomy has been performed on the involved side without great benefit. The purpose in subjecting children with this disorder to such a radical surgical procedure is to prevent, if possible, the severe osseous deformities that develop on the involved side rather than to try to influence the scleroderma. The scleroderma tends to involute while the bones and other structures on the involved side cease to grow.

DR. OLIVER S. ORMSBY As to terminology, I agree that Dr. O'Leary's description is correct. I have seen a number of children with superficial sclerodermatous lesions on the trunk, but none had this peculiar sclerodactylia-like involvement of the hand.

PSEUDOXANTHOMA ELASTICUM (DARIER) ASSOCIATED WITH FORMATION OF BONE
Presented by DR. B. B. BEESON

This woman, aged 52, states that her cutaneous trouble has been present for ten years. A general physical examination gave essentially negative results.

The skin is relaxed and hangs in folds about the neck, axillae, abdomen and thighs. There appears to be a network of yellowish papules, which are, however, not elevated.

Microscopic examination revealed clumping and swelling of the elastic fibers. Bony formation and calcification were present, the groundwork of some of the calcified areas being composed of interwoven elastic fibers. The sections were examined by Dr Jaffe and Dr Civatte, both of whom observed the formation of bone.

DISCUSSION

DR CLARK W FINNERUD At a previous meeting Dr Nomland and I presented a patient with pseudoxanthoma elasticum, and we have been studying the case from the standpoint of the calcium content of the elastic tissue. Since that time we have studied another case of that condition. In view of the fact that there is no specific stain for calcium, hematoxylin being as good as any other stain, we decided to measure quantitatively the amount of calcium in tissue affected with pseudoxanthoma. We have found that whereas in normal skin the calcium content is approximately 1 per cent, in these two cases it was 5 and 6 per cent. Apparently in cases of pseudoxanthoma elasticum most of the calcium is deposited in the elastic tissue. This may also be true of other similar conditions that have not yet been studied. I think there is no question about the diagnosis. This is not formation of bone, as stated by Dr Beeson, but marked deposition of calcium in the degenerated elastic tissue.

DR O H FOERSTER, Milwaukee It is interesting that this patient, who presents an extensive example of the disorder, was said not to show the angioid streaks. A patient recently seen by us, in whom the condition has certainly existed no longer than six months, definitely showed angioid streaks.

DR CLARK W FINNERUD In our series my co-workers and I are reporting a case of pseudoxanthoma with angioid streaks, one of pseudoxanthoma without the streaks and one of angioid streaks without pseudoxanthoma elasticum.

DR B B BEESON The most extensive review of this disorder is that by Surmont. In his series of about thirty cases, calcification was present in three

ERYTHEMA AB IGNE Presented by DR. E A OLIVER

This white woman, aged 24, for the past four years has complained of dryness and scaliness of the skin of the eyelids accompanied by an eruption of styes.

She has been treated at various times with hot compresses of boric acid and with radiant heat.

The skin of both upper eyelids is mottled, showing a light brown reticulated pigmented erythema, the reticulation is quite marked.

DISCUSSION

DR HENRY E MICHELSON, Minneapolis I believe that a biopsy should be made. My clinical diagnosis is lichen planus but of course that would have to be verified by a microscopic examination. I recently saw a patient who had a residual melasmic staining confined to the eyelids which on section proved to be lichen planus. The rest of the body was completely clear.

DR OLIVER S ORMSBY What application of heat was made?

DR CLARK W FINNERUD I wonder whether the hyperpigmentation was not accentuated by the absorption of the ammoniated mercury which was used?

DR E A OLIVER The patient is now using an ointment containing yellow mercuric oxide locally and is taking quinine. Several years ago she was treated by an ophthalmologist for recurrent styes. While she was in the hospital hot compresses of boric acid were applied to the lids, and she received radiant heat. I admit that I did not consider the diagnosis of lichen planus. Dr Senear saw the patient with me several times, and as he presented one of the first cases of lichen planus of the eyelids before this society he naturally would have considered that possibility. Dr Senear and I believe that this is a clearcut case of erythema ab igne.

DR OLIVER S ORMSBY I knew Dr Oliver was going to present a patient with this diagnosis, and in view of the fact that this disorder is supposed to be produced by fire I wish to show a photograph of a perfectly classic erythema ab igne with pigmentation following hot applications in a patient with herpes zoster

LIVEDO RETICULARIS Presented by DR M H EBERT

This woman, aged 40, presents a bluish red reticulation over the extensor surfaces of the arms and forearms, the dorsa of the hands, the calves and the buttocks, there is also a slight involvement of the scapulae. The eruption presents the same pattern as cutis marmorata but it is more violaceous and does not disappear when the body is warm or during the summer. The color disappears on pressure with the diascopé but returns slowly. There is no palpable infiltrate in the lesions. They cause no sensation. The patient has a chilblain circulation of the hands, feet and nose. Her sister has a similar pattern of cutis marmorata, which is transitory and appears only when she is chilled. The patient's eruption appeared ten years ago, two years after she started to work in a fruit store where the atmosphere was always cold and damp. Her father became paralyzed when he was in his forties. The patient has been married for several years but has never been pregnant. There is no evidence of syphilitic infection.

A series of injections of neoarsphenamine had no effect on the skin. Repeated Wassermann tests have been negative. The patient exhibited a negative reaction to an injection of full strength of a purified protein derivative of tuberculin. Her basal metabolic rate when she was first seen, over a year ago, was -12 per cent. It was brought up to normal by the administration of thyroid, but this had no effect on the disorder. Her blood pressure has varied from 140 to 160 systolic and from 90 to 100 diastolic. Her only additional complaint is nervousness.

DISCUSSION

DR M H EBERT I did not have the opportunity in presenting the patient to state that the Wassermann reaction was negative and that the result of injection of arsphenamine is negative so far as the lesions are concerned. The tuberculin test was also negative, and roentgenograms of the chest showed no abnormalities, hence two most common causes of livedo, i e., syphilis and tuberculosis, are ruled out. Cases have been reported in which the livedo reticularis was associated with arteriosclerosis, and others in which it occurred in association with what is called an anomaly of the blood vessels. This woman presents no evidence of arteriosclerosis, except a slight elevation of the blood pressure, the systolic pressure being from 150 to 160. Her father died of apoplexy when in his early forties. Her sister has a similar cutaneous condition.

Erythema ab igne has the same anatomic basis as livedo reticularis, i e., a slowed-up circulation producing this peculiar pattern.

CREeping ERUPTION Presented by DR RUBEN NOMLAND

This man, aged 28, states that he acquired his disorder in Bermuda two months ago. It originally manifested itself as itching lesions on the scrotum and thighs which appeared after the patient had spent only a few hours on the beach. In its progress one of the lesions on the left thigh moved at least 8 inches (20 cm) in a straight line, and probably twice as much in all, from the point of its origin. Within the past four days it has progressed more than 1 inch (2.5 cm).

There are many inflammatory vesiculopapules on the scrotum and several lesions on each thigh. Several active burrows—circuitous red lines ending in a vesicle—can be seen running along the thighs for a distance of from 1 to 6 cm.

DISCUSSION

DR OLIVER S ORMSBY For several years this disorder was considered rare. One or two cases of it were observed in Philadelphia. I had never observed one,

but Dr Kirby-Smith reported a series of two or three hundred. The disorder is comparatively common in the southern and southwestern parts of this country.

DR WILLIAM ALLEN PUSEY I can confirm what Dr Ormsby has just said. I spoke to Dr Kirby-Smith recently, and he told me that in Florida the disorder is not rare. The larva which causes the condition was first pictured by a Russian in a free hand drawing, but no one else has been able to recover the organism. It was so long before any one could locate it that his observation was impugned. When I was writing the first or second edition of my textbook on dermatology I received a letter from a country physician in Montana who said that he had observed one case of creeping eruption in which a lesion progressed right across the eyelid and that he had recovered the organism. He sent me photomicrographs of the organism which exactly duplicated the drawing made by the original observer. As far as I know, this physician was the first in this country to recover the larva.

DR RUBEN NOMLAND The members probably know that Dr Bedford Shelmire studied this disorder and proved that the creeping eruption which occurs in the South is caused by the larva of the hookworm which infests cats (Shelmire, Bedford. Experimental Creeping Eruption from a Cat and Dog Hookworm [A. Braziliense], *J A M A* 91 938 [Sept 29] 1928).

SUPERFICIAL EPITHELIOMA Presented by DR M H EBERT

This man, aged 64, presents an eruption on the upper portion of his left leg which, he states, appeared thirteen years ago as a small rough spot which gradually enlarged. It has caused him no inconvenience.

There is a dollar-sized plaque with a slightly elevated dull red border made up of small nodules. The center is slightly depressed, atrophic and deeply pigmented.

Histologic examination of tissue from the margin disclosed a superficial basal cell epithelioma.

XANTHOMA MULTIPLEX Presented by DR T K LAWLESS

This infant, aged 5 months, at birth was free from all manifestations of cutaneous disorder. A week or ten days later there appeared on the head and face an eruption consisting of pale yellow to yellowish brown papules and nodules of various sizes and shapes. The lesions were firm and painless on pressure. The entire picture was progressive, both as to the areas involved and as to the size of the lesions. There is no history of diabetes or disease of the gallbladder in the family, although during the past two years the child's father has been incapacitated because of glomerulonephritis.

The histologic picture is typical of xanthoma. The results of chemical examinations of the blood are shown in the tabulation.

	Mg per 100 Cc of Plasma		
	First Determination 1/15/36	Second Determination 1/31/36	Normal Values (Adult)
Total cholesterol (Bloor's saponification method)	104	83.3	150 — 190
Lipoid phosphorus	10.3	11.3	7 — 14
Lipoid lecithin	259	282.9	175 — 330
Total cholesterol (Okey's digitonin method)	80.6	98.25	135 — 120
Free cholesterol	31.35	31.35	40.5 — 103
Total fatty acids (Bloor's method)	473.55	361.9	290 — 420

DISCUSSION

DR CLARK W FINNERUD I know that several other members think, as I thought in the beginning, that the disorder is urticaria pigmentosa with xanthoma-like lesions, but there was no urtication, and the sections ruled out that diagnosis. I also thought of nevoxantho-endothelioma, but I think that the sections ruled out that diagnosis also. I think that this disorder is of the type described, chiefly

by Artz, as juvenile xanthoma. In the disorder which he described the histologic picture was essentially identical with that in this case. The sections contained a large number of multinucleated giant cells.

PURPURA WITH ANNULAR LESIONS Presented by DR E P ZEISLER

This white woman, aged 40, presents a purpuric eruption of two weeks' duration on the lower extremities and lower portion of the abdomen. She states that she had taken iodides before this eruption appeared and that she also used feenamint. The urine at one time showed sugar, but it has been normal recently.

Examination of the blood gave normal results. Some of the lesions have enlarged and involuted to form annular purpuric patches.

DISCUSSION

DR HENRY E MICHELSON, Minneapolis. I venture the diagnosis of purpuric pigmented lichenoid dermatitis. I realize the danger of making this diagnosis, for the knowledge regarding this condition is not complete. My opinion is that in most instances the individual lesions look like Schamberg's disease, and the proportion of purpuric punctae, papular lesions and pigmentation varies considerably. I believe that whatever causes the trouble affects the blood vessels and allows extravasation with a varying degree of infiltration. Since I have become interested in this subject I have seen a number of cases, and in most of them the eruption begins to fade in the center of the plaque and gradually disappears completely. I believe that the condition exhibited by Dr Zeisler's patient can be classed under this heading.

DR RICHARD S WEISS, St Louis. This patient states that she took potassium iodide. I have seen several patients who exhibited a purpuric eruption following the use of potassium iodide, and I wonder whether or not this drug has played a part in causing this patient's eruption.

DR E P ZEISLER. I am glad to hear Dr Michelson's remarks. I thought it best to present the patient without committing myself as to the type of purpura. Whether purpuric lichenoid dermatitis is to be classified as a distinct clinical entity has not been decided, and it will probably remain an open question, at least until further clinical reports are available.

THE FOX-FORDYCE DISEASE Presented by DR E A OLIVER

This Negress, aged 43, who was treated for syphilis at the clinic of St Luke's Hospital during the past three months has complained of an annoying pruritic papular eruption in both axillae.

In both axillary fossae there are discrete papules, from the size of a pinhead to that of a small lentil, they are sharply defined and are present in rather large numbers. There are no lesions in the pubic region.

DISCUSSION

DR E A OLIVER. I hoped this presentation would bring forth some discussion, for I do not know how commonly the Fox-Fordyce disease occurs in Negroes.

DR RICHARD S WEISS, St Louis. I have seen three cases of Fox-Fordyce disease in Negroes.

DR F E SENEAR. About five or six years ago a Negress with the Fox-Fordyce disease was presented before this society (ARCH DERMAT & SYPH 18 788 [Nov] 1928). That patient was unusually intelligent and temperamentally was the kind of person in whom that disease is apt to occur. Later I learned from Dr Weiss that the disease occurs in Negroes.

DR S W BECKER. I had occasion recently to review some work regarding the skin of Negroes, and I came across the statement that the apocrine glands, the involvement of which is characteristic for the Fox-Fordyce disease, are about three times as numerous in Negroes as in white persons.

A CASE FOR DIAGNOSIS (MULTIPLE IDIOPATHIC HEMORRHAGIC SARCOMA [KAPOSI]?)
Presented by DR F E SENEAR, DR M R CARO and DR EARL R PACE

This girl, aged 18, was presented before this society in October 1932 (ARCH DERMAT & SYPH 27.851, [May] 1933) The lesions had appeared two weeks previously following a dislocation of the right ankle

During the past three years, in spite of considerable roentgen therapy, the lesions have continued to extend, at present they involve both sides of the right ankle

A CASE FOR DIAGNOSIS (IDIOPATHIC MULTIPLE HEMORRHAGIC SARCOMA [KAPOSI]?)
Presented by DR THEODORE CORNBLEET and DR EARL R PACE

This man, aged 26, an American of Polish descent, first noted a tender "pimple" on the lower portion of the right leg He presented himself at the clinic of the Cook County Hospital in August 1935, exhibiting a dusky red lesion the size of a half palm above the external malleolus, at about one-third the distance to the knee The lesion lacked infiltration at that time, except near the center, where it was somewhat elevated and presented a small, crusted, granulomatous area which appeared to be an indolent pyogenic ulcer Antiseptic local applications seemed only to free it of pustular discharge In September it was noted that the entire patch was becoming infiltrated, that it was rather sharply margined and that very little of the color was removed by pressure with the diascope

The results of a biopsy made in September 1935 were reported by Dr Caro as follows The epidermis showed a thin, non-nucleated scale, acanthosis of the rete mucosum, a thickened granular layer and an intact basal layer The papillary and subpapillary layers of the corium showed proliferation of young blood vessels surrounded by a diffuse infiltration of histiocytes, much brown pigment—which occurred free and within cells—and many extravasated erythrocytes Chromatophores were present about the deeper blood vessels and were scattered diffusely through the corium Staining for iron showed dense deposits of hemosiderin in the upper part of the corium and about the deeper blood vessels and sweat glands and a smaller amount scattered throughout the tissue

During November and the early part of December the patient received intensive roentgen therapy, and during the past seven weeks he was ordered to remain in bed so as to remove any elements of stasis The lesion has lost most of its infiltration, but it has extended somewhat, and the color remains about the same

The results of a biopsy made at the Cook County Hospital on Dec 2, 1935, were reported as follows There is capillary angiomatosis of the entire cutis, with extension into the subcutaneous tissue and marked deposits of blood pigment The covering epidermis shows acanthosis and hyperkeratosis

DISCUSSION

DR F E SENEAR The young woman presented has large ulcerating lesions on the outer aspect of the ankle We had not thought of Kaposi's sarcoma as the diagnosis, but the section, as Dr Caro saw it, indicated that disorder at the time the patient was presented before the society, and, as I remember, Dr Michelson and Dr Montgomery agreed with the pathologic diagnosis, but Dr Finnerud did not The patient was given roentgen therapy The lesions on the outer side of the right ankle have not extended, and the ulceration and vegetative character have been considerably reduced The lesion on the inner aspect of the ankle has ulcerated

The second patient was seen at the Cook County Hospital by Dr Cornbleet and Dr Pace, and the picture he presents is similar to that exhibited by the young woman Neither of the patients presents manifestations which we regard as signs of Kaposi's sarcoma, and the patients are presented not with that diagnosis but rather as exhibiting a pathologic picture which apparently is compatible with a diagnosis of Kaposi's sarcoma

DR CLARK W FINNERUD I believe that in the young woman there is a chronic hypostatic process, an old lichenified patch on one side and what amounts to a varicose ulceration on the other A chronic hypostatic condition like this is not

uncommonly responsible for extravasation of blood pigment, which histologically is present in the cutis, and also for the change in the blood vessels. The picture in the young man is somewhat similar. I believe that the young woman does not have Kaposi's sarcoma, and I am not at all sure that the man has.

PEMPHIGUS OF THE SENEAR-USHER TYPE WITH ORAL LESIONS Presented by
DR E P ZEISLER

This man, aged 50, has had for seven years recurring bullous lesions in the mouth and on different areas of the body, chiefly on the chest, back, axilla and groin and in the anal region. The involvement in the mouth is acute, the lesions are painful and soon become covered with a pseudodiphtheritic membrane. The cutaneous bullae at present are few and have become crusted. Those around the anus have assumed a vegetating character. There has been no appreciable loss of weight, and there are no marked constitutional symptoms.

A recent examination of the blood showed 5,010,000 erythrocytes, 7,000 leukocytes and 80 per cent hemoglobin. The results of the differential count were as follows: polymorphonuclears, 74 per cent, lymphocytes, 20 per cent, monocytes, 1 per cent, eosinophils, 2 per cent, and basophils, 3 per cent. Smears from the mouth showed diphtheroids, streptococci, a few Vincent bacilli and no Monilia.

Treatment has consisted chiefly of administration of various forms of arsenic and of tryparsamide. Recently there has been some improvement as a result of oral administration of acetarsone.

The patient was formerly under Dr Oliver's care, who presented him before this society four years ago (ARCH DERMAT & SYPH 23 995 [May] 1931).

The patient has also recently taken some tablets of erythrol tetra-nitrate in doses of $\frac{1}{2}$ grain (0.0324 Gm) with some benefit.

DISCUSSION

DR E A OLIVER I disagree with the diagnosis of pemphigus of the Senear-Usher type. I believe that the disorder is pemphigus vulgaris. I presented this man before this society about five years ago with the diagnosis of pemphigus of the mucous membranes. He was under my care for about a year, and during that time was given the Davis treatment and injections of tryparsamide. In July 1935 he returned, at that time his mouth was badly involved and he had lesions on the body. For about three months he took one-half grain of erythrol tetra-nitrate twice daily. This, I believe, helped him considerably.

DR RICHARD S WEISS, St Louis Erythrol tetra-nitrate has been suggested by Dr Cyril McBryde as a remedy for pruritus. It was used especially in the treatment of dermatitis herpetiformis and of the pruritus associated with jaundice, and some good results were obtained, but I have not heard of its being used in treatment of pemphigus. The improvement of pemphigus by the Davis treatment, I believe, is due to the arsenic rather than to the coagulating preparation used. In a certain percentage of the cases if sufficient arsenic can be introduced into the system, improvement and sometimes cure results. Pollitzer's solution, consisting of sodium arsenate, 1 Gm, phenol, 1 Gm and distilled water, 50 cc, injected intramuscularly in doses of 1 cc daily or every other day seems to be as efficient as iron cacodylate. Other forms of arsenic, such as tryparsamide, may also give good results. I have had one patient, as Dr Ormsby and Dr O'Leary may recall, a woman with a severe pemphigus vegetans, who recovered completely after taking huge doses of viosterol by mouth and has remained well over a period of about three years.

DR E P ZEISLER I am glad to hear Dr Oliver dispute my diagnosis. I am always reluctant to make a diagnosis of the Senear-Usher type of pemphigus, but the long duration of the disorder in this case does not fit in with the duration in most cases of pemphigus, and I thought that the relatively benign course might justify the diagnosis pemphigus of the Senear-Usher type. At about the same time Dr Oliver prescribed erythrol tetra-nitrate I was giving the patient acetarsone. It would be interesting to know which did him the most good.

PHILADELPHIA DERMATOLOGICAL SOCIETY

VAUGHN C GARNER, M.D., *Secretary*

Jan 17, 1936

HERBERT J SMITH, M.D., *Chairman*

LUPUS ERYTHEMATOSUS Presented by DR JOSEPH V KLAUDER

H M, a man aged 45, presents confluent erythematous patches of twenty-three years' duration on the left side of the face and over the entire left ear, which is shrunken and atrophic. The scalp and mouth are normal.

DISCUSSION

DR FRED D WEIDMAN I agree with the diagnosis. However, there are two other possibilities: lupus vulgaris erythematodes and porokeratosis of Mibelli. Casual inspection gives the impression that the margins of the lesions are elevated, but in my opinion analysis shows that their conspicuousness is due to the marked atrophy present in their central parts. By pressure I was not able to elicit anything that looked like the special focal infiltrations of tuberculosis. The location of the disorder around the ear calls to mind a patient whose case Dr Corson reported and who was presented at two or more national meetings of dermatologists. That patient had an area of atrophy around the ear, extending thence over the scalp, and a diagnosis of possible granuloma annulare was made. I think that in that case eventually the disorder turned out to be porokeratosis of Mibelli. The reason I mention this is that one should be open minded in regard to lesions occurring around the ear and extending over the scalp and showing elevated margins. The eruption exhibited by Dr Klauder's patient presents a degree of scaliness in the center which is not compatible with a diagnosis of porokeratosis of Mibelli.

DR EDWARD F CORSON This patient undoubtedly has lupus erythematosus. I do not believe that the disorder closely suggests anything else. The patient to whom Dr Weidman referred was presented about ten years ago at meetings of the American Dermatological Association and at the Atlantic Dermatological Conference and caused considerable discussion as to the diagnosis. Finally the diagnosis of sarcoid was agreed on. There is a picture in Andrews' textbook under the title of sarcoid which represents the nearest approach to the disorder in that particular case I have ever seen. At one of these meetings a wide range of diagnoses was offered. Dr Gilchrist after looking at the sections thought that the disorder was epithelioma, Dr Wise regarded it as granuloma annulare, some one else diagnosed it as pigmented lupus vulgaris. No two members agreed on the same diagnosis.

DR JOHN H STOKES Of late I have found it helpful to be highly suspicious of inflammatory processes that occur along the edge of the concha of the ear and down behind it. I think that a nickel dermatitis is one of the few new dermatologic diagnoses in recent years, and its association with pyogenic and seborrheic infections of the scalp, nose and ears sometimes produces pictures that are deceiving and easily overlooked. This combination of an inflammatory process around the ear and over the area of the nose which comes in contact with spectacles deserves to be looked into. I noticed that this patient has the mark of the bridge of spectacles over his nose. The possibility that the disorder may be due to the metal in the spectacles should be kept in mind even if the patient is not wearing spectacles at the time of examination or states that he does not use glasses, forgetting that he does when he reads.

A CASE FOR DIAGNOSIS Presented by DR H J GOLDMAN

L P, a Negress aged 39, states that about fifteen years ago nonpruritic papules developed on the left knee. They spread down the leg slowly but dis-

appeared completely after the patient received fifteen intravenous injections of a drug, the name of which she does not know. They were present for five years before this treatment was administered. After eight years they recurred on the left knee and spread to the extent seen at present. This second eruption is pruritic and greatly excoriated. It has been present for two years, having extended slowly. The general physical condition of the patient is normal.

A provocative test of the blood after injection of neoarsphenamine gave several negative Wassermann, Kahn and Eagle reactions. One test, however, showed a positive Eagle reaction. Several tests with various antigens made since have been negative. No examination of the spinal fluid has been made. A biopsy report from Dr. Weidman's laboratory stated that the pathologic picture was not that of syphilis, psoriasis or parapsoriasis. The patient received injections of neoarsphenamine totaling 12 Gm, which resulted in questionable improvement, one-half skin erythema dose of roentgen radiation brought about no change in the condition.

DISCUSSION

DR J M SCHILDKRAUT, Trenton, N J. I suggest the diagnosis of syphilis.

DR CARROLL S WRIGHT. I think one ought to be able to rule out that diagnosis on the basis of the repeatedly negative reactions and the lack of response to antisyphilitic therapy. I believe that the disorder is a tuberculous process.

DR JOHN H STOKES. I could not decide what the lesion was, but I think that two other things should be considered: (1) ichthyosis hystrix and (2) a factitious eruption which the patient has maintained over a long period, not necessarily as a malingerer but unconsciously as a minor traumatization. I think that these two things are worth including in the discussion, but frankly I can not decide what the disorder is.

DR FRED D WEIDMAN. The biopsy does not show anything that would indicate any particular dermatologic entity. One of the members informally mentioned lichen planus this evening, and because of the variable histologic picture which lichen planus may present, depending on its stage, I should say that in this case the histologic picture is more compatible with that than with tuberculosis or syphilis. There is no evidence of an important degree of cellular infiltration, and taking all the factors into consideration I think that the disorder resembles nontypical lichen planus more closely than it does any other disease. However, the distribution is not at all what one expects to see in lichen planus. When I first saw the patient I thought of certain conditions which Dr. Schamberg had seen, namely, a condition on the thighs of young men in which the infiltration is much more marked than that exhibited by Dr. Goldman's patient and in which areas of atrophy occur between the patches. One must remember the possibility of traumatism playing a part. The one case which I observed was in an athlete—a hurdler. I always believed that these apparently fibrosarcomatous lesions have a tuberculous basis, and as it is known that tuberculosis can produce a great range of changes it is possible that it may induce fibrous changes in the skin. I am inclined to regard this patient's disorder as atypical lichen planus, but I should like to hear more satisfactory suggestions.

ANTHRACOSIS OF THE SKIN. Presented by DR PATRICIA DRANT

H K, a man, presents anthracotic markings on the left shin which appeared after application of activated charcoal in the treatment of a chronic ulcer of the leg. The ulcer is completely healed.

DISCUSSION

DR FRED D WEIDMAN. This patient was treated with activated charcoal over a period of many weeks in the Philadelphia General Hospital. The ulcer

was the size of a palm or larger when he first received that treatment, and I did not see him again until the entire lesion had become epithelialized. Then to my astonishment I noticed these linear anthracotic markings of the skin. They corresponded to the margins of the ulcer and my opinion is that portions of the charcoal became sequestered under the margins of the regenerating skin. This is a rather unusual illustration of another (therapeutically induced) method whereby anthracosis of the skin may develop. The disorder is known to appear on the faces and hands of miners, to follow injury with gunpowder and to develop after a similar type of trauma. One should add activated charcoal to the list of substances that should not be applied to the skin therapeutically. This condition parallels those in which pigmentation of the face followed the use of lead subacetate in the treatment of ivy poisoning, the salt becoming reduced to metallic lead.

DR SIGMUND S. GREENBAUM: Activated charcoal has a beneficial effect on some lesions. In this case no harm results from this type of pigmentation, as it is concealed from ordinary view and occurs in an aged subject. Of course, it would be extremely embarrassing in a woman or in a young person.

A CASE FOR DIAGNOSIS Presented by DR HERBERT J. SMITH

E. C., a boy aged 10 years, presents a confluent acuminate follicular eruption involving the pilosebaceous orifices. It is inflammatory at times and is most marked on the extremities. In April 1934 the patient had German measles, the rash disappeared in one week, but the skin remained dry and rough. The patient had been healthy as a baby, and his skin had been normal until April 1934. When he was first seen, in July 1935, the keratosis was more marked than at present.

DISCUSSION

DR THOMAS BUTTERWORTH, Reading, Pa.: I think that in this case the age of the patient, the grouping of acuminate follicular papules, some of which are inflammatory and some of which contain small hairlike spines, and the fact that the eruption is especially marked on the extremities support a diagnosis of lichen spinulosus. When I first saw this patient about all I could do was to classify the disorder among the hypertrophies of the skin. I ruled out pityriasis rubra pilaris because of the absence of involvement of the scalp and nails and the absence of the characteristic spines over the fingers, and in my opinion the disorder is lichen spinulosus.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I agree with the diagnosis of lichen spinulosus.

DR. JOHN H. STOKES: I think there are several possibilities that should be further considered and more carefully investigated. One is lichen scrofulosorum. Occasionally it is associated with tuberculosis of the joints. A careful investigation for latent tuberculosis is indicated. The grouping which one sees in the ordinary lichen scrofulosorum is sometimes lacking. Another possibility is a dermatophytid. I have never forgotten the extremely unpleasant experience I had when Dr. Fred Harris found a dermatophytic process in the nails of a young girl with an eruption that strongly suggested pityriasis rubra pilaris. Removal of the finger-nails and cleaning the process about the nail beds caused the eruption to clear. In children these dermatophytids are occasionally the sequels of extremely small foci of dermatophytosis, therefore, careful search should be made, and one should not too readily despair if one does not find the organism the first time. The scalp particularly ought to be searched. Occasionally the dermatophytid long precedes the appearance of a kerion. The kerion suddenly appears on the scalp months after the child has shown the first signs of an almost exfoliative dermatitis. Moreover, some of the children with this disorder are extremely ill, showing toxic symptoms, elevation of temperature, and so on, before the focus of fungous infection is found. I also wish to call attention to the fact that over the front of the thorax this boy has something

besides follicular papules. He has the flat, more or less characteristic invisibly scaling papules of pityriasis lichenoides chronica. In some cases of parapsoriasis mixtures of types of lesions occasionally occur. At least three different types may appear in the same patient, hence I believe that the appearance on the front of the thorax of these flat, shiny papules which show no scale until they are abraded and then fluff up into a mass of scales is suggestive of that possibility. I think that a good deal of study of this boy's condition must be done before any of these diagnoses is accepted.

DR FRED D WEIDMAN. Some of the lesions show quite a good picture of lichen spinulosus, particularly if examined with a pocket lens. I am certain that the disorder is not pityriasis rubra pilaris. I believe, too, that there is something else on the skin besides the simple lichen spinulosus. What it is I do not know. I should like to make more investigations in respect to this other condition. At first I thought that possibly the additional lesions over the posterior part of the trunk and also over the upper parts of the chest were resolving eczematous lesions, but in one examination such as could be made tonight one cannot ascertain that. Resolving lesions of scabies may present an appearance similar to that exhibited by this patient, hence a great deal depends on the nature of the lesions of scabies in respect to the resolving lesions of eczema. One must have all the data before one can make a final pronouncement.

DR JOHN H STOKES. In my experience when an extensive follicular keratotic eruption is present one must also consider lichen planus. That may sound rather surprising, but in lichen planus there can be a range of lesions which one frequently forgets entirely, or one may forget that it is possible to have, in addition to typical flat angular shiny papules with pseudo-arsenical keratoses in the palms, keratosis pilaris, lichen spinulosus, and so on, and whenever lesions of lichen spinulosus appear the possibility of lichen planus should be considered in making the differential diagnosis.

INTERSTITIAL KERATITIS Presented by DR JOSEPH V KLAUDER

H M, a girl aged 11 years, when first seen in November 1935 had interstitial keratitis involving the right eye of one week's duration. There was diffuse haziness of the entire cornea. The patient had received no treatment. With the site under local anaesthesia a piece of the cornea was excised, it was studied by the following methods: dark field examination, Levaditi's stain for spirochetes and intratesticular and intracorneal inoculation of rabbits. *Spirochaeta pallida* was not demonstrated by any of these methods. The rabbits were inoculated two months ago, hence they are still under observation.

INTERSTITIAL KERATITIS TREATED WITH QUININE BISULFATE WITHOUT EFFECT Presented by DR JOSEPH V KLAUDER

S M, a girl aged 9 years, was first seen in October 1935, presenting severe interstitial keratitis involving both eyes. For two weeks she was given 2 grains (0.13 Gm) of quinine bisulfate three times a day, without effect. Treatment with bismuth was then started and was effective. The patient has a peg-shaped tooth with a suggestion of a notched cutting surface. Quinine was administered by mouth in view of Schereschewsky's report (*Klin Wchnschr* 14 381, 1935) concerning the beneficial effect of quinine administered orally to patients with interstitial keratitis. Schereschewsky also reported a spirocheticidal effect of quinine in experimental syphilis in apes and in treatment of interstitial keratitis in syphilitic rabbits. In addition to employing quinine in the treatment of a patient with interstitial keratitis I studied the possible spirocheticidal action of the drug in syphilitic rabbits. It was observed that 20 mg of quinine hydrochloride per kilogram of body weight administered intravenously was the lethal dose for rabbits. The animals survived an intravenous injection of 18 mg per kilogram. An intravenous injection of 15 mg per kilogram given to a rabbit with well pronounced testicular syphiloma

had no effect on the syphilitic lesion, as ascertained by dark field examination, or on the clinical course of the syphiloma

INTERSTITIAL KERATITIS IN MOTHER AND CHILD (SYPHILIS IN THE THIRD GENERATION) Presented by DR JOSEPH V KLAUDER

FIRST GENERATION—The grandmother, aged 45, has a definite history of an eruption of secondary syphilis which occurred soon after her marriage. She received little treatment at the time, she had one miscarriage but no children born dead. She has one daughter. There were other siblings. The husband died of cancer. The Wasserman reaction of his blood was negative during the last illness. The woman showed no clinical evidence of syphilis. The Wassermann reaction of her blood was 11—, the Meinicke reaction was 43.

SECOND GENERATION—The daughter was aged 19 at the time of onset of bilateral interstitial keratitis. The clinical diagnosis was confirmed by examination with the slit lamp. There were no other stigmas of congenital syphilis. The Wassermann reaction was 444, and the Meinicke reaction, 44. She gave birth to one dead child and has one living daughter. The Wassermann reaction of her husband's blood was 444, and the Meinicke reaction, 44. This patient is now 25 years old. She was married at the age of 17.

THIRD GENERATION—The granddaughter is $6\frac{1}{2}$ years old, at the time of onset of interstitial keratitis she was $2\frac{1}{2}$ years old. The examination with the slit lamp confirmed the clinical diagnosis. The Wassermann reaction was 4442, and the Meinicke reaction, 44. The luetin test was positive. Clinical examination gave essentially negative results except for the fact that one upper incisor is peg shaped, it is regarded as a Hutchinson tooth. There is a retinochoroiditis which is regarded as being of syphilitic origin.

DISCUSSION

DR JOSEPH V KLAUDER The presence of a positive Wassermann reaction in the husband of the patient in the second generation complicates the interpretation. The grandmother asked me not to disclose the nature of the disease to her daughter and her husband, hence I could not question the husband regarding the source of infection. Did the husband infect his wife, in whom interstitial keratitis developed later? If so the woman presents a rare instance of interstitial keratitis in acquired syphilis. Granting that the wife has congenital syphilis, did she infect her husband? This is not likely. I believe that the positive Wassermann reaction of the husband's blood has no relation to his wife's infection but is purely coincidental. If one accepts interstitial keratitis as proof of congenital syphilis, then the child exhibits an instance of syphilis in the third generation. It is to be noted that the mother (second generation) had a typical interstitial keratitis at the age of 19 and that she was married at about the age of 17. This brings up the following important question. Does the early marriage of patients with congenital syphilis whose infection is untreated favor the transmission of the infection to their progeny? It is reasonable to believe that under these circumstances infection is more likely to be transmitted than if marriage is longer delayed.

DR JOHN H STOKES I have no comment to make except that I think that this is a remarkable combination and that the evidence of syphilis in the third generation comes as close to being air tight as possible, much closer than in most cases. I think that there is a tendency to report cases as instances of syphilis in the third generation without adequate evidence, but that certainly is not the case in this presentation.

DR SIGMUND S GREENBAUM I am glad that Dr Klauder mentioned the possibility of the husband's superinfecting the wife. I have observed instances of superinfection in patients with congenital syphilis. In this presentation the extraordinary thing, I think, is the fact that both the mother and the child had interstitial keratitis—as though the cornea was the weak place in the make-up of each of these patients.

DR THOMAS BUTTERWORTH, Reading, Pa I have read an abstract in which an ointment containing a small amount of quinine was described as being used in treating interstitial keratitis I also read an article recommending roentgen therapy to the cornea for the treatment of interstitial keratitis Has Dr Klauder used either of them?

DR JOSEPH V KLAUDER I have used quinine locally in the treatment of interstitial keratitis too recently to draw any conclusions I have never used roentgen therapy in treating that disease I gather from the literature that the results were not sufficiently impressive to offset the risk inherent in roentgen radiation The case in which I removed a piece of cornea is representative of a group of three cases in which a piece of cornea was removed but did not disclose *S pallida* This seems to indicate that the organism is not present at the site of the interstitial keratitis The fact that interstitial keratitis may appear after fairly thorough treatment seems to me additional evidence against the hypothesis that the organisms are present in the cornea

DR JOHN H STOKES I have always believed that there was some doubt about the presence of the organisms in the cornea

DR JOSEPH V KLAUDER I inoculated the cornea as well as the testicles of a rabbit with spirochetes and obtained negative results The rabbits are still under observation The time since inoculation is about two months

DR FRED D WEIDMAN About the premises in interstitial keratitis I am not informed, but from analogy I should say that it would be unusual if *S pallida* were to be demonstrated in interstitial keratitis It is known how difficult it is to demonstrate the spirochetes even in active gumma, and in the other phases of syphilis, namely, in the diffuse fibrous one, it is even more difficult to recover the organism I doubt, therefore, that these negative results of histologic studies or even of experimentation with rabbits indicate that the spirochetes are not present The negative results merely show the well known difficulty of demonstrating the organisms in old syphilitic lesions

DR JOSEPH V KLAUDER The point is that all the methods used gave negative results—dark field examination, inoculation of animals and staining

DR SIGMUND S GREENBAUM I agree with Dr Weidman The negative results do not at all exclude the possibility of the organisms' being present I have inoculated rabbits with many types of tissue and have obtained only negative results The point is that those rabbits have to be watched over a period of four or five months before negative results can be reported

A CASE FOR DIAGNOSIS Presented by DR JOSEPH V KLAUDER

I K, a man aged 51, presents on the anterior aspect of the upper surface of the tongue an irregularly shaped ulcer 4 cm long and 2 cm wide with a yellowish surface and a raised undermined edge There are confluent ulcerations on the tip and two ulcerations on the lower surface of the left side of the tongue Clinically the condition is not malignant No other dermatoses are present The patient states that about two months before the ulcers appeared he had bitten his tongue An ulcer appeared, which never entirely healed The patient is undernourished, he has lost 10 pounds (4.5 Kg) in six months As he was seen for the first time today complete investigations have not been made

DISCUSSION

DR SIGMUND S GREENBAUM I suggest the diagnosis of tuberculous ulcers

DR FRED D WEIDMAN I think that some tissue should be stained for the organism if that has not been done

DR JOSEPH V KLAUDER It was done this afternoon

DR FRED D WEIDMAN Of course, it is in lesions of the mouth rather than in those of the pharynx or of the tongue that the organisms are found in cases of

superficial tuberculosis They are much more commonly found there than on the skin proper The patient exhibits a remarkably cleancut, punched-out ulcer There is scarcely any infiltration, and the edges are not necrotic or shaggy I thought that the necrotic tissue on the base of that ulcer was quite thin, so much so in fact that I thought I could make out the outlines of the architecture of the muscular tissue of the tongue underneath There is little active tissue around that lesion If such a condition were to occur on the skin I should say that the lesion was a type of trophic ulcer I agree with Dr Greenbaum, but I should be very chary of making a diagnosis of tuberculosis at this time The patient ought to be examined neurologically to see whether there is any basis for the lack of reaction

DR SIGMUND S GREENBAUM Of course when I suggested the diagnosis of tuberculosis I did not mean to make a diagnosis before the results of laboratory examination are reported

DR JOSEPH V KLAUDER The biting of the tongue mentioned in the history apparently was slight I do not believe that it is of any significance

PITYRIASIS ROSEA-LIKE ERUPTION OCCURRING DURING BISMUTH THERAPY Presented by DR THOMAS BUTTERWORTH, Reading, Pa

D B, a Negro aged 61, received twelve injections of bismuth subsalicylate, after which there appeared on the trunk an eruption consisting of oval, scaly and crusted lesions with their long axis along the lines of cleavage The first patch appeared on the flexor aspect of the left elbow The eruption appeared about Sept 1, 1935, and changed little in the succeeding four months During that time the bismuth therapy was continued There is a bismuth line on the gums

DISCUSSION

DR JOHN H STOKES I am inclined to agree with Dr Butterworth's diagnosis It seems to me that the chronology makes it unlikely that the eruption is a manifestation of recurrent syphilis, of syphilis that is resistant to bismuth or of an infection which has appeared during the course of the bismuth therapy, hence I think that the interpretation of reaction to bismuth is probably correct Some of the lesions seem somewhat more scaly than those resulting from bismuth therapy and look as if they showed some atrophic changes, possibly associated with some granulomatous infiltration However, as the primary infection occurred so long ago and as there is no reason for regarding the infection as of a relapsing type or for considering the disorder a secondary eruption coming on in a period of bismuth activation or in spite of bismuth, I agree with the diagnosis

DR ROBERT L GILMAN I agree with the diagnosis

DR EDWARD F CORSON I wonder whether the lesion on the lip does not play some part in the symptomatology While there is no information as to its features, it is possible that it may have been an initial lesion The syphilis which is said to have been present before antedates the Wassermann test, and I am not sure that it can be proved that the patient had syphilis at that time The lesions which he exhibits now are merely suggestive of a rupial type of syphilis It is possible that the patient presents one of those rare instances of a second infection after a cure or that this is his first infection with the disease The history is inadequate

DR THOMAS BUTTERWORTH, Reading, Pa Dark field examination of material from the granuloma which was present on the lip when the patient was seen showed no spirochetes The lesion looked so much like an epithelioma that a biopsy was made The pathologic report was nondescript In the meantime the Wassermann reaction of the blood was reported to be positive, and the diagnosis of gumma was considered to be correct In about three or four weeks the lesion involuted The appearance of these cutaneous lesions brought up the question whether the disorder was pityriasis rosea complicating syphilis or whether the eruption was due to the

bismuth, and the treatment was continued much longer than the disorder warranted. The patient applied for treatment in September, and he was given bismuth whenever he came to the clinic. If the eruption recurs he will be presented again.

DR H J GOLDMAN The disorder at first examination suggested either epithelioma or syphilis. The patient was subjected to a therapeutic test with bismuth for three or four weeks, and the lesion involuted about 10 per cent. He has since received roentgen therapy, as a result of which the eruption has involuted.

DR ROBERT L GILMAN I recall that the report on the biopsy stated that the lesion was of a nonspecific type, and at that time Dr Butterworth and I thought that possibly the biopsy specimen did not really represent the growth. Rather than jeopardize the man further, however, we sent him to the radiotherapy department for treatment. I do not recall whether at the time we thought there was a bona fide epithelioma, but we thought there might be and considered it best to regard the lesion as such. I think that the syphilitic infection is indubitably of longer duration than six or seven months.

A CASE FOR DIAGNOSIS (DERMATITIS REPENS? DERMATOPHYTOSIS?) Presented by
DR CARROLL S WRIGHT

K. A., a woman aged 56, states that in December 1934 a "pus" infection developed around a heavy callosity on one sole. It gradually spread to involve the sole and the top of the foot, intense soreness and swelling resulting. The lesion was treated by the family physician with dyes and ointment containing salicylic acid, but no improvement resulted. The lesion failed to improve after application of wet dressings of boric acid, potassium permanganate and solution of aluminum acetate. It was intolerant to ointments except zinc oxide paste with no salicylic acid. At present the left foot is somewhat edematous. The dorsal surface is slightly reddened and crusted. The sole is almost entirely denuded of epithelium, it has a fungating appearance in certain areas, and in other areas it is eroded and crusted. There is no pustulation. The borders are scaling and undermined in places. A report on the laboratory examination stated that fungi had been found at one time but that none were demonstrable at present. Ordinary staphylococci were present, no yeasts were found. There was no sugar in the urine.

DISCUSSION

DR CARROLL S WRIGHT The first time I saw this patient was in consultation with the family physician, who had been using an ointment containing a concentration of strong salicylic acid, the foot looked badly blistered and exhibited a good deal of pus. I regarded the lesion as an overtreated fungous infection and prescribed compresses of potassium permanganate and a simple paste containing boric acid. I have seen the patient only at rare intervals. On the first occasion I took some scrapings which disclosed no fungi, but a check-up was impossible.

DR DAVID M SIDLICK There are many features about the disorder which suggest a late manifestation of syphilis. I understand that a serologic test has been negative, but I think that a thorough therapeutic test should be made.

DR JOSEPH V KLAUDER I should not subscribe to the diagnosis of syphilis. I should consider the possibility of a malignant process and have a biopsy made. There is no outstanding condition that I have in mind as resembling this disorder.

DR JOHN H STOKES First I thought of Madura foot, but later, under better lighting and in a somewhat altered position, I was impressed by the possible malignant aspect. It seems to me entirely possible that this patient has a diffuse carcinomatosis or sarcomatosis of the foot, which may have originated, as she describes it, in a chiropodist's tinkering with a lesion of some sort on the foot. It may have been a melanomatous growth. I have seen feet infiltrate without visible metastasis and become again half as big as they were originally from a nevus between the first and second toes which had been unnoticed. I should say that that

possibility is the most critical one in this case and calls for immediate biopsy. In my opinion syphilis would be the least likely possibility. An extensive fungous or fungous-pyogenic infection with cellulitis and elephantiasis change would be worth considering. One or two of the flat squamous lesions on the toes looked unusually like keratosis blennorrhagica, but one or two lesions do not justify a diagnosis. One might consider a pustular psoriasis and the resistant phenomenon—mycotic, pyogenic, whatever it may be—which Barber in England and Andrews in this country have described. The quicker this patient enters a hospital and has a specimen removed for biopsy, the sooner an accurate diagnosis will be reached.

DR SIGMUND S GREENBAUM. On the dorsum of the foot are small elevations suggestive of the lesions seen in cases of melanoma. I agree with Dr Stokes that the most likely diagnosis is malignant degeneration.

DR FRED D WEIDMAN. I think that syphilis can be clinically excluded in this case. From the appearance of the foot one gets the impression that the process is proceeding from the center of the entire foot and enlarging it generally in all directions, as occurs in maduromycosis. Certainly the appearance of the sole and of the toes sticking out like big pegs in front—the foot evidently would not rest on the toes at all—bears out this impression. Of course, there is only the history to indicate that this remarkable enlargement has been present for two weeks. It may have been present for longer than that. In any event the progress of the lesion has been fast. I think that such rapid progress rather speaks against carcinoma, it reminds one more of sarcoma. And the type of the tissue—rather bright red—is more suggestive of sarcoma than of carcinoma. I think that a biopsy should be made and that roentgen examination should ascertain whether there is destruction of the osseous tissue in the interior of the foot. Exhaustive studies of the blood should be made, it is possible that the disorder is lymphoblastoma. I think it may turn out to be sarcoma, as a second possibility I should consider lymphoblastoma.

DR CARROLL S WRIGHT. I noticed the scar on the patient's lip the first time I saw her, and after leaving the house I discussed with the family physician the possibility of an old syphilitic infection, and he told me he had treated the patient for many years. I suggested that she be given more bismuth, but this was not done until I saw her again this fall. I gave her about six injections, and the foot has not improved. In fact, in the last week it has become much worse. Therefore I believe that the possibility of this lesion's being in any way related to a syphilitic process can be ruled out.

NOTE.—Scrapings showed no fungi. A biopsy showed a specific infectious granuloma on the order of tuberculosis. The pathologic diagnosis was possibly "frambesia."

INTERSTITIAL KERATITIS TREATED WITH MALARIA. Presented by DR JOSEPH V KLAUDER

C D, a youth aged 19, was first seen in February 1934, complaining of interstitial keratitis affecting the left eye. Malaria therapy was given, and he had ten consecutive rises of temperature to 106 F. He received no other treatment. There was a definite improvement in the interstitial keratitis. After this a few injections of a bismuth preparation were given. The patient then took a self-prescribed rest for two months. A short time later there was involvement of the right eye and still later a recurrence of the disorder in the left eye. The case demonstrates involvement of the second eye with interstitial keratitis and relapse in the first eye after malarial treatment of interstitial keratitis.

DISCUSSION

DR JOHN H STOKES. I wish to ask Dr Klauder whether he has ever seen instances of malaria in congenitally syphilitic children precipitating interstitial keratitis?

DR JOSEPH V KLAUDER. No, I have not.

BRONX DERMATOLOGICAL SOCIETY

HENRY SILVER, M D, *Secretary**Regular Meeting, Jan 23, 1936*EUGENE F KELLEY, M D, *President*

A CASE FOR DIAGNOSIS (SYPHILITIC ONYCHIA?) Presented by DR SAMUEL FELDMAN

J F, a shoemaker aged 52, says that he is not aware of having a venereal disease His wife had no miscarriages The Wassermann and the Kahn reaction of the blood were 4 plus

The nails show longitudinal ridges and irregular pitting The edges are brittle and separated from the nail bed The nail of the ring finger of the left hand shows a yellowish white area surrounded by a red rim, which is plainly visible through the healthy transparent portion of the nail plate The entire area appears to be somewhat depressed below the surface of the nail and gives the impression of a circumscribed syphilitic papule On the anterior surface of the left thigh there is a firm, painless swelling with a deep perforation in the center

DISCUSSION

DR ARTHUR SAYER I believe that a diagnosis of syphilitic onychia cannot be made on purely clinical grounds, psoriasis, eczema and tinea must also be considered The therapeutic test should settle the question of a syphilitic onychia

DR MARION B SULZBERGER I do not see how the therapeutic test can settle the diagnosis, since psoriasis and syphilis respond to the arsenical medication I think that if the lesion on the leg is caused by syphilis it is in all probability a manifestation of tertiary syphilis, and it would be unusual to find lesions of the nails or syphilitic papules under the nails at the same time The latter usually appear in early or in late stages of secondary syphilis I agree that there is no pathognomonic picture of psoriasis of the nails except perhaps the typical psoriatic papule which is present underneath the nail Jadassohn stated that the crescent-shaped subungual hyperkeratosis of the nail bed at both sides and near the free edge is a fairly characteristic manifestation of psoriasis of the nail, more so than stippling

DR ADOLPH ROSTENBERG My conception of syphilitic onychia is that it is a dystrophic change This patient presents a heaped-up lesion which fits more with the diagnosis of psoriasis or tinea than with that of syphilitic onychia

DR SAMUEL FELDMAN I doubt that this patient's disorder is syphilitic onychia, that is why the diagnosis is presented with a question-mark Heller described as a syphilitic papule of the nail bed a condition similar to that exhibited by this patient Because of this similarity and of the associated gumma of the thigh and the positive Wassermann and Kahn reactions, the diagnosis of syphilitic onychia must be strongly considered

A CASE FOR DIAGNOSIS (LICHEN PLANUS OF THE NAIL BED?) Presented by DR MARION B SULZBERGER

M W, a saleswoman aged 35, has suffered from diabetes mellitus for the past five or six years, requiring from 60 to 80 units of insulin daily At present the diabetes is not entirely controlled by insulin and diet

The eruption appeared on the dorsum of the right hand in the summer of 1933 and gradually spread to almost all parts of the body When the patient was first seen, in July 1935, there was typical widespread lichen planus on the arms, legs, trunk and back In addition, there were macerated whitish red plaques of lichen

planus about the anus and vulva. No lesions of the nails were noted. Topical applications were prescribed, and the patient was advised to have daily injections of solution of sodium arsenate.

When the patient was next seen, in January 1936, the cutaneous lesions were considerably improved, but the perianal and perivulvar lesions were unchanged. It was then noted that several nails on both hands were short and irregularly broken off. There was bluish subungual discoloration at the distal end of the affected nails beneath the broken nail plate.

DISCUSSION

DR LOUIS CHARGIN It is possible that the disorder is lichen planus of the nails. There is no reason that a nail affected with lichen planus may not appear as a spoon nail. In two cases which I observed recently, one of which was presented before this society (*ARCH DERMAT & SYPH* 33 1096 [June] 1936) there was no resemblance to the appearance of this patient's nails. Lichen planus of the nails develops slowly, whereas the involvement of the nails in this case has been rather rapid. There are no characteristic features of lichen planus of the nails. The diagnosis can be accepted if the lesions of the nails disappear simultaneously with the eruption of the body.

DR MARION B SULZBERGER I agree with the remarks made by Dr Chargin, but I wish to add some facts which were not brought out sufficiently in the history. This patient had widespread, disseminated typical lichen planus of the body when I first saw her in 1933. As a result of arsenical treatment and mild topical applications the condition cleared up sufficiently for the patient to forego further treatment until last week. At that time there was an exacerbation of lichen planus, and the patient claims that the lesions of the nails started to appear simultaneously with those of the skin. I do not know whether the disorder was discernible under the light tonight, but beneath the nails there are several discrete circumscribed papular and macular reddish blue discolorations. This feature and the history of the development of the lesions led me to believe that the disorder may be lichen planus of the nail bed.

DR LOUIS CHARGIN In the two cases of lichen planus of the nails which I observed the manifestations in the nails were associated with palmar lesions. The association is more than a mere coincidence. Cases of lichen planus of the palms and hence also of lichen planus of the nails are comparatively rare.

A CASE FOR DIAGNOSIS (MYCOSIS FUNGOIDES? LYMPHOBLASTOMA?) Presented by DR H B FEILER

C K, a woman aged 35, presents a fairly generalized eruption of five months' duration. It is especially marked on the face, ears, trunk, arms and buttocks. The chest and abdomen are comparatively free from lesions. The eruption consists of confluent dusky red infiltrated patches, which include many areas of various sizes and patches of normal unaffected skin. The infiltration of the face is nodular. The dorsal aspects of both hands are studded with pea-sized yellowish nodules. The patient experiences difficulty in closing the hands.

There are marked loss of hair and erythema of the scalp but no visible infiltrations. There is no enlargement of the glands, though the inguinal glands are palpable. The liver is slightly enlarged, and the spleen is not palpable. The patient complains of severe itching and burning.

The blood count showed 72 per cent hemoglobin, 4,100,000 red cells and 34,900 white cells. The results of the differential count were as follows: polymorphonuclears, 48 per cent, monocytes, 2 per cent, eosinophils, 2 per cent, myelocytes, 2 per cent, normocytes, 1 per cent, and lymphocytes, 45 per cent.

Histologic examination showed that the stratum corneum was uniformly thin and nonnucleated. The epidermis was about eight cell layers thick, and there was a tendency toward flattening out of the rete pegs, obliterating the papillae of the corium. Scattered cells in the prickle cell layer showed intercellular edema with pyknosis of the nuclei. The intercellular bridges were uniformly distinct. The

entire corium in all its layers showed a diffuse increase in fibrous tissue and numerous collections of cells in foci, mainly perivascular. These collections of cells consisted of round cells, an occasional plasma cell and eosinophil and also large pale stellate cells of the reticular type. There was no indication that the cutaneous lesion had resulted from leukemic infiltration of the skin. The histologic picture was consistent with the diagnosis of mycosis fungoides.

DISCUSSION

DR ARTHUR SAYER. I believe that the high white blood cell count, the moderate adenopathy and the infiltration on the face speak in favor of leukemia and against mycosis fungoides.

DR DAVID BLOOM. The eruption on the extensor surfaces of the arms and on the trunk, with clearcut areas of healthy skin between violaceous infiltrated lesions, strongly suggests mycosis fungoides. However, the nodular eruption on the eyebrows and at the angles of the mouth presents the characteristic features of leukemia. The latter, together with the high leukocyte count and the lymphocytosis, suggest to me the diagnosis of leukemia in spite of the lack of adenopathy.

DR WILBERT SACHS. Mycosis fungoides is one of the conditions which is included in the group of lymphoblastoma. It is not always possible to differentiate which entity it is. According to the biopsy, however, the disorder is not lymphatic leukemia. The histologic picture points more to mycosis fungoides.

DR FRANK E. CROSS. It is known that in lymphoblastoma a biopsy of material from one part of the body may show mycosis fungoides while one of material from another area may show another form of lymphoblastoma. This patient's disorder may be one in which this combination exists. The picture does not suggest typical mycosis fungoides but rather leukemia.

DR CLINTON H. MARTIN. The hard, drawn, thickened skin of the hands which almost suggests scleroderma of the palms and fingers would fit in more with the diagnosis of lymphoblastoma.

DR MARION B. SULZBERGER. In reference to the histologic and the hematologic picture lymphatic leukemia has been mentioned. According to the hematologic report the disorder is not lymphatic leukemia but myeloblastic leukemia. Cutaneous lesions occur rarely in myeloblastic leukemia and when they do occur they often present a variegated appearance.

DR ARTHUR SAYER. The point to be emphasized is that the patient suffers from lymphatic leukemia and yet the clinical picture looks like mycosis fungoides. This would be in agreement with Symmers (*ARCH. DERMAT. & SYPH.* 25:1 [Jan] 1932), who on the basis of many autopsies concluded that disorders diagnosed during life as mycosis fungoides were proved at autopsy to be Hodgkin's disease, leukemia or lymphosarcoma.

DR PAUL GROSS. In speaking of leukemia one should be more specific. In this case the disorder is leukaemia cutis propria. The diffuse infiltration on the face is typical of that condition, and although the lesions on the arms and body are suggestive of mycosis fungoides, their symmetrical distribution and diffuse infiltration point to leukemia. It is by no means necessary for a typical leukemic blood picture to be present in early stages of primary leukemia of the skin, and the blood count in this case points only to a rapidly progressing leukemia of the lymphatic type. Clinically there is no evidence of myelogenous leukemia.

DR LOUIS CHARGIN. This patient exhibits deep-seated infiltrations on the trunk with numerous clear areas, a picture which as a rule indicates mycosis fungoides. The section shows a multiplicity of cell types. Therefore, the clinical and the histologic picture fit in well with the diagnosis of mycosis fungoides. The face, however, shows infiltrations, a feature which is not seen in mycosis fungoides but

is observed in disorders belonging to the leukemia group. If the infiltrations on the face are to be considered lymphatic leukemia, the blood picture should corroborate the diagnosis. The blood picture in this case is not incompatible with, but is by no means typical of, lymphatic leukemia. Moreover, one would expect an adenopathy, and that is lacking. While this patient shows characteristics of two diseases, no one disease can be singled out. Perhaps this fits well with the point brought out by Dr Sayer in respect to Symmer's studies.

DR ADOLPH ROSTENBERG The condition may start clinically like mycosis fungoides and later assume the character of lymphosarcoma or leukemia. A case which I had the opportunity to observe exemplified the difficulty in diagnosis. The patient, whom I presented before this society, had large tumors suggesting melanomas, which, however, yielded rapidly to roentgen treatment. This led me to suspect leukemia. The blood picture, however, was entirely normal for eight months. Eventually the patient died. But shortly before death the blood picture became typical of lymphatic leukemia. In the patient presented tonight the lesions of the body look like mycosis fungoides. The lesions of the face fit in well with the picture of leukemia. I suggest roentgen treatment for diagnostic purposes.

DR SAMUEL M. PECK Perhaps this subject is being complicated unnecessarily. The clinical appearance certainly suggests mycosis fungoides, histologically there is some basis for this diagnosis also. If one wishes to maintain that the lesions on the face are those of lymphatic leukemia, that assertion should be based on some histologic proof. In the presence of an atypical histologic picture the hematologic picture should be the basis of the diagnosis. A competent pathologist, such as Ludwig Pick, of Berlin, Germany, has often stated that histologically it is almost impossible to make a differential diagnosis between aleukemic leukemia and lymphosarcoma. There are, however, certain criteria which help to make a differential diagnosis between these conditions. In mycosis fungoides there is a marked polymorphous infiltration and large clear cells are present. In lymphosarcoma and aleukemic leukemia there is a monomorphous type of cellular infiltration. In lymphosarcoma the cutaneous lesions more closely resemble those of a lymph node than in aleukemic leukemia. I mean by that that there is a more definite stroma in addition to the cells. In my opinion there is no definite hematologic picture in mycosis fungoides. In this case I think that an examination of the blood should be made by a competent hematologist.

DR H. B. FEUER The lesions on the face and hands are more infiltrated than in mycosis fungoides. The deeper infiltrations and the hematologic picture suggest lymphoblastoma.

RECKLINGHAUSEN'S DISEASE IN A NEGRO BOY Presented by DR ISIDORE M. LASHINSKY

This 7 year old Negro boy came to the Harlem diagnostic clinic of the Board of Health on Jan 5, 1936, presenting tumors scattered over the body. His mother stated that the first tumor appeared on his back in the sacro-iliac region about four years ago. The patient, the elder of two children, was born normally at term. There is no history of consanguinity.

The patient is poorly nourished, he presents about one hundred tumors covering the trunk, extremities and face. The tumors are freely movable and skin colored, and the majority vary in size from that of a pea to that of a walnut. The largest tumor is situated in the sacro-iliac region and is the size of a lemon. Almost all the tumors are hard and tender to the touch, the largest is soft and lobulated and is not only tender but at times painful. There are definite café au lait spots on the right side of the chest below the axilla, on the posterior aspect of the right arm, on the right scapula, on the right thigh and on both buttocks. The child is mentally retarded.

Physical examination gave negative results. The urine was normal. The Wassermann reaction of the blood of the mother and of that of the child was negative.

Histologic examination confirmed the diagnosis of Recklinghausen's disease.

DISCUSSION

DR LOUIS CHARGIN The whole picture, including the large tumor, is that of Recklinghausen's disease

DR PAUL GROSS The tumor on the back is extremely firm and large. Many of the smaller nodules present the same firmness. Although the clinical picture indicates Recklinghausen's disease, one should exclude the diagnosis of a more malignant growth, especially that of a neurogenic sarcoma.

DR HARRY KEIL Before the diagnosis of Recklinghausen's disease is accepted, that of fibrolipoma should be ruled out by biopsy. The large tumor on the back apparently consists of a number of nodules of about the same consistency as the discrete lesions. If the disorder is Recklinghausen's disease it is of the fibromatous type.

DR MARION B. SULZBERGER I have seen few cases of Recklinghausen's disease in Negro children. It seems to me that in this case the tumors are too hard to be lesions of Recklinghausen's disease, moreover, in no places are there any tabs or protruding soft tumors. The lesions lie beneath the skin and lack the usual herniation. Furthermore, while there are some pigmented nevi, one cannot class them with certainty as café au lait spots. The tumors in this case are tender and even painful, that is not the usual finding in Recklinghausen's disease. In addition to this, the large, hard tumor located on the back is distinctly lobulated, which is another unusual feature. Whether Recklinghausen's disease may take on this form in Negroes, I do not know, but I cannot subscribe to that diagnosis in this case without knowing the results of a histologic examination.

DR HENRY SILVER All the criteria necessary for a diagnosis of Recklinghausen's disease are present: the usual small and large tumors of various consistency, the larger pigmented spots and the spots which would be café au lait on a white skin but on Negro skin are necessarily darker. I agree with Dr. Gross that the large, firm tumor may be malignant. In rare instances malignant tumors have been observed in association with Recklinghausen's disease.

DR SAMUEL FELDMAN In some conditions diagnosed as Recklinghausen's disease there may be no other lesion than café au lait spots or there may be in addition one or two small tumors or nevi. There is no combination of lesions that is not possible in that disease. In a certain case one may see a large number of tumors of one type and an insignificant number of or no tumors of another type. As far as the size of the tumor is concerned, I wish to recall a case of Recklinghausen's disease in which the diagnosis was proved by histologic examination which I presented before this society several years ago, in that case there was a large tumor on the abdomen in addition to numerous small lesions.

DR SAMUEL M. PECK I wish to point out that several of the lesions which this patient presents are uncommon in ordinary Recklinghausen's disease. I am referring to the lesions in the supraclavicular region of the right side, which are freely movable hard nodules. In the broad sense Recklinghausen's disease shows a tendency to a certain type of nevoid formation which seems to be closely related to the nerves and pigmentary system. That is why neurofibromas and even melanomas are encountered. The tumors found in patients with Recklinghausen's disease are varied, and several types of tumor may be present in one patient.

DR ISIDORE M. LASHINSKY I do not doubt that malignant degeneration may occur in a case of Recklinghausen's disease, but the large tumor on the back has existed for four years, and in view of this it can hardly be regarded as malignant.

A CASE FOR DIAGNOSIS (URTICARIA PIGMENTOSA WITHOUT PIGMENTATION [PARKES WEBER]? PARAPSORIASIS [JULIUSBERG]?) Presented by DR LOUIS CHARGIN

I A, a salesman aged 40, presents an eruption of eight months' duration. It appeared first on the sides of the trunk and later spread to other parts of the

body The lesions are small reddish macules and have persisted since the onset of the disorder There is no itching The lesions do not urticate to any extent on irritation There is practically no pigmentation

DISCUSSION

DR LOUIS CHARGIN There are two points to be stressed 1 The eruption clinically resembles urticaria pigmentosa, and yet there is little or no pigmentation and the lesions do not urticate 2 Parapsoriasis must be considered as a possibility Urticaria pigmentosa without pigmentation has been described under various names I present this patient as exhibiting a disorder of the type described by Parkes Weber

DR THEODORE ROSENTHAL I agree with the diagnosis of urticaria pigmentosa with or without pigmentation Some of the lesions on the body appeared fairly well pigmented

DR SAMUEL FELDMAN I could not see any pigmentation However, the appearance of the lesions fits in with the picture of urticaria pigmentosa, and lesions of this type with slight pigmentation are not uncommon in that disease I am inclined to accept a diagnosis of urticaria pigmentosa, although it is impossible to rule out parapsoriasis without a biopsy

DR DAVID BLOOM In spite of the lack of pigmentation I am inclined to accept the diagnosis of urticaria pigmentosa The eruption has been present for only eight months, and it is possible that pigmentation will appear later In parapsoriasis the picture is quite different The peculiar mottling and the psoriasiform lesions seen in parapsoriasis are absent in this case

DR ISIDORE M LASHINSKY About three years ago I presented before this society a patient with urticaria pigmentosa acquisita in whom the manifestations were identical to those exhibited by Dr Chargin's patient When the eruption first appeared the lesions were of the same hue as the ones in this patient, being erythematous and not pigmented, but they did urticate However, I fully agree with the diagnosis of urticaria pigmentosa

DR ADOLPH ROSTENBERG I agree with the diagnosis of urticaria pigmentosa The only doubtful point is that in early stages of the disease there should be some urtication which this patient's lesions do not show

DR PAUL GROSS It is difficult to make a diagnosis in view of the lack of pigmentation and the absence of a convincing urticarial reaction On the other hand, there are small lichenoid papules on the flexor surface of the forearms and on the inner surface of the arms besides a few slightly scaly reddish macules which may point to the diagnosis of parapsoriasis

DR LOUIS CHARGIN If the disorder were typical urticaria pigmentosa there would be no special reason for presenting the patient The fact is that the lesions are not pigmented and do not urticate In disorders of this type as described by F Parkes Weber (*Brit J Dermat* 42:374, 1932) mast cells have been found, but thus far I have been unable to obtain material for a biopsy There are some papules on the forearms, one or two of which show some scaliness, and it is that which suggests the possibility of parapsoriasis of the Juliusberg variety

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ALEUKEMIC RETICULOSIS

AN ADDITIONAL MEMBER OF THE GROUP OF SO-CALLED
CUTANEOUS LYMPHOBLASTOMAS

JAMES T WAYSON, MD

HONOLULU, T H

AND

FRED D WEIDMAN, MD

PHILADELPHIA

To the great majority of American dermatologists the term cutaneous lymphoblastoma conveys a certain definite clinical picture. It consists usually of a preliminary diffuse dermatitis (generalized scaly erythrodermia) succeeded by a tumor-like stage (*granuloma fungoides sensu stricto*). It is the clinical phase which commands the scene. Promptly after the appearance of the clinical manifestations, however, the picture becomes associated with disease of the lymphoid apparatus. Therefore, considerations of this subject must be arranged into, and must revolve around, two fields: (1) the essentially dermatologic and (2) the hematopoietic.

It is not urgent to discuss the former field because dermatologists are so familiar with it, but at present there is real need for better understanding of the precise scope of the lymphoblastoma. The rôle of the lymphocyte in particular is implied, for if the suffix is removed from "lymphoblastoma" only "lymphoblast" remains. Indeed it was the original intention of Mallory¹ to attach to the lymphoblastomas the sense of a malignant tumor process with only the lymphoblast as the cell performing. Warthin² followed his lead in nomenclature. In speaking of mycosis fungoides he said: "In the great majority of cases this disease is a small-celled lymphoblastoma." Yet if one pries into the premises a little more inquisitively one finds that Warthin vitiated

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Read before the Section on Dermatology and Syphilology at the Eighty-Seventh Annual Session of the American Medical Association, Kansas City, Mo., May 13, 1936.

1 Mallory, cited by Krumbhaar¹⁰

2 Warthin, A. S. The Genetic Neoplastic Relationships of Hodgkin's Disease, Aleukaemic and Leukaemic Lymphoblastoma, and Mycosis Fungoides, *Ann Surg* 93:153 (Jan) 1931.

such an exclusive rôle for the lymphocytic series when he included Hodgkin's disease among lymphoblastomas in general. In this light, then, there is a conflict between the etymology of "lymphoblastoma" and the range of cell types included in the various dermatoses constituting the group of cutaneous lymphoblastomas. Nevertheless, it appears fitting to concede that the term lymphoblastoma in the sense in which it was used by Warthin pertained to lesions in which it was essentially the lymphocyte which was concerned.

Twelve years ago Keim³ formally introduced the term lymphoblastoma to American dermatologists in connection with a case of universal leukaemia cutis. Five years later he reported twenty cases under the same designation. In the interim Fraser⁴ reported two cases of mycosis fungoides in which he was finally able to establish the diagnoses of lymphatic leukemia and lymphosarcoma. He affirmed Keim's opinion of the "genetic relation between mycosis fungoides, lymphatic leukemia and lymphosarcoma" but at the same time stated a preference for the name reticulum cell sarcoma rather than lymphosarcoma. This indicated at least that he recognized the participation of the reticulo-endothelial system likewise in mycosis fungoides, i e., that he believed that mycosis fungoides was not exclusively a lesion of the lymphocyte.

Dermatologists are thus justified in taking Keim's two papers as base-lines (singularly, the first paper antedated Warthin's communication by seven years), with Frazer's paper interposed. If one follows Keim's theory there is little recourse but to accept the scope of cutaneous lymphoblastoma as he indicated it, as he and Warthin, to say nothing of Wile, were of the same Michigan school. There must have been the closest understanding between these three workers. Of lesser importance for present purposes is the fact that all lymphoblastomas, cutaneous or other, were emphatically classified as neoplastic processes—not as infections. It is significant in this connection that reticulosis was not mentioned in any case, evidently reticulum, if present (as in cases of Hodgkin's disease), was regarded as the reactive, normal stroma of the tissue which was being invaded by the supposedly neoplastic lymphocyte. Thereafter, Keim's statements, "the multiple clinical pictures associated with true lymphadenoses should be

3 Keim, H. L. Universal Leukemia Cutis, *Arch Dermat & Syph* **10** 579 (Nov) 1924, The Lymphoblastomas, *ibid* **19** 533 (April) 1929.

4 Fraser, J. F. Mycosis Fungoides, *Arch Dermat & Syph* **12** 814 (Dec) 1925.

5 Some hematologists at least hold a similar opinion. Pepper and Farley (*Practical Hematological Diagnosis*, Philadelphia, W. B. Saunders Company, 1933, p. 443) said of mycosis fungoides in their text: "It is probable that the hemopoietic disorder is primary, and the condition should be diagnosed according to the blood picture and the mycosis fungoides considered a secondary phenomenon."

regarded as the variable cutaneous expression of the lymphoblastomas,"⁶ and "the constant pathologic condition in all is a cell of the lymphocyte series" were sufficiently definite, and they narrow the considerations to cells of the lymphocyte series, although it must be pointed out at once that this statement pertains only to the circumstances present in Keim's twenty cases

In Keim's series little additional help, except in a negative way, was given from the observations on the bone marrow, although this is briefly described in some of his cases. The blood pictures too are described only briefly. We are of the opinion that in this large series of cases neither the blood nor the bone marrow was studied exhaustively in respect to cell types as considered by modern hematocytologists and that the observations are therefore not quite adequate to exclude the reticuloses from the lymphoblastomas. Future reports of cases of granuloma fungoides and of lymphoblastoma in general will be more valuable for analysis if the details of cytology of the blood, bone marrow, spleen, liver and lymph nodes are recorded in the splendid way in which both Loveman and Mercer reported their observations in their cases of leukemic reticulosis.

The preceding sentences are not intended as a criticism of the scope of the hematopoietic studies of the Michigan school, but they indicate that from the point of view of pathology the way is still open to include other members of the hematopoieses among the lymphoblastomas constituting Keim's series. If this can be done, it remains only to establish a similar set of clinical circumstances and join them with some vice of the blood-forming organs in order for the disease to qualify as a member of the group of lymphoblastomas. We believe that this can be done in the case which we report. We are of the opinion that the presence of a premycotic stage followed by a tumor stage and death satisfies the clinical requirements. Thereafter the profound alterations met in blood-forming tissues at necropsy, whether they are regarded as manifestations of atypical Hodgkin's disease, lymphosarcoma or reticulosis, complete the requirements of the lymphoblastomas.

We urge the reader to note the faithfulness with which the full scope of the pathologic changes of granuloma fungoides was exhibited on the skin of our patient, as illustrated by photographs. Incidentally, such was not the case in the instances of leukemic reticulosis (monocytic leukemia) reported by Mercer⁶ and by Loveman,⁷ who have so fully discussed the latter disease.

⁶ Mercer, Samuel T. The Dermatoses of Monocytic Leukemia, *Arch Dermat & Syph* **31** 615 (May) 1935

⁷ Loveman, Adolph B. Monocytic Leukemia Cutis, *South M J* **29** 357 (April) 1936

REPORT OF A CASE

Course—P M, a 36 year old Filipino living in Hawaii, H I, exhibited a generalized scaly erythroderma which began in November 1931. At first there was a patch of itchy dermatitis above the interscapular region, within a few days this extended to cover the entire body. Particularly affected were the face, ears and interscapular, antecubital and popliteal regions. The palms and soles alone were not involved. The lesions consisted of large slightly infiltrated furfuraceous and crusted erythematous plaques which were intensely pruritic. When the lesions were cleaned a raw red weeping surface remained. After three weeks of treatment by soothing measures the patient was discharged much improved.

In August 1932, i e, nine months later, there was a mild recurrence accompanied by pruritus. In October the type of eruption changed, this time it involved both cheeks, the anterior portion of the chest, the extensor surface of both arms and the inside of the thighs. The lesions did not itch. They were discrete irregular reddish brown patches. The patient had been gradually losing weight, and he complained of malaise and weakness.

The cervical, axillary, epitrochlear and inguinal lymph nodes were slightly enlarged and firm but not tender. There were crepitant râles at both apexes posteriorly, and moderately advanced pulmonary tuberculosis was demonstrated. The spleen was enlarged, firm and tender. The ulnar nerves were palpable and somewhat tender, there appeared to be a greater wasting of the thenar, hypothenar and interosseous groups of muscles than could be accounted for by muscular inactivity. Neurologic examination revealed no abnormality in the sensory or motor system or in the reflexes.

There was thus a preliminary diffuse dermatitic stage extending, with one remission, over a period of one year. Then, promptly after the patient's admission to the hospital, widely generalized macules and subcutaneous nodules developed. The first, which were dime-sized, slightly elevated and bluish red, were located on the thoracic region. Their appearance was preceded by fever, the temperature reaching 101 F, which persisted until the patient's death.

The distribution of the subcutaneous swellings was similar to that of the diffuse eruption which preceded them, i e, they were present over the ears, cheeks, middle of the forehead, tip of the nose, extensor surfaces of the arms, upper parts of the chest, both anteriorly and posteriorly, inner aspect of the thighs and legs. They varied in size, one on the right cheek being as large as a pigeon egg. They were fairly firm, dusky or livid and not ulcerated. Eventually they became firmly attached to the skin.

During the third week of the tumor stage symptoms of laryngeal edema necessitated tracheotomy. There was intermittent swelling of the wrist and joints, associated with severe pain over the joints and over the small bones of the hands and feet. In spite of repeated blood transfusions, roentgen therapy and hypodermic administration of iron and arsenic, the patient became progressively more anemic and toxic. He died on Jan 27, 1933, after a slight pulmonary hemorrhage, in the fifteenth month of the disease and the ninth week of the tumor stage.

Laboratory Studies—The Wassermann and Kahn tests of the blood were negative. The number of red blood cells was always below 3,000,000. There was moderate leukopenia. The percentage of polymorphonuclears averaged from 65 to 89, that of mononuclears, 2, and that of lymphocytes, 9. Abnormal cells were not observed.

Tubercle bacilli were noted in the sputum on three occasions, they were established as such by inoculation of guinea-pigs. A culture of the blood gave negative

results Repeated smears from the nose and from snips of tissue from lesions, including the subcutaneous nodules, did not show Hansen's bacillus The non-protein nitrogen content of the blood was 27.2 mg per hundred cubic centimeters, the uric acid content was 3.5 mg, and the sugar content, 106 mg The urine contained albumin and casts but no Bence-Jones protein

Histologic sections of skin, subcutaneous nodules and cervical lymph nodes exhibited similar features, namely, groups of endothelial-like cells which in the cutaneous sections were just beneath the intact epithelium There were zones of round cells in alveolar-like arrangement, varying in size, shape and staining intensity There was no evidence of a purely inflammatory involvement, and the histologic picture did not resemble that of granuloma The histologic diagnosis was lymphosarcomatosis

Roentgen Studies—In the chest in addition to signs of fibroid tuberculosis there was definite widening of the superior mediastinum, which was doubtless referable to glandular enlargement The sternum, clavicle and ribs were normal In the



Fig 1—Tumor stage just before death

skull there was definite rarefaction in the left frontoparietal and to a slight degree in the occipital region The posterior sutures were widened The left foot showed two or three slight periosteal elevations, generalized atrophy due to disuse and moderate rarefaction of the medullary canal in the proximal phalanx of the middle toe There was definite destruction of bone in the second phalanx of the great toe The hands showed corresponding changes There was rarefaction of the medullary canal of all the phalanges and metacarpals, the change being particularly at the extremities but extending into the medullary canal of most of the bones There was destruction of the distal end of the first phalanx of the middle finger Some of the metacarpals exhibited sclerosis in places As to the radius and ulna, there was slight destruction of bone at their lower extremities, on both the right and the left side, and the rarefaction extended into the medullary canal There was periosteal thickening at the middle Roentgenograms of the pelvis showed only sclerosis of the left sacro-iliac joint, the vertebrae were normal

In short, there was clearcut evidence of infiltration of both the cortex and the medulla, with actual destruction of bone in some places The bones of the toes, hands and wrists suffered most, but the skull and tibia were also involved

Gross Postmortem Examination—The patient was markedly emaciated. The subcutaneous nodules were firm and grayish white on the surface of the sections. There was a cavity in the upper part of the right lung showing signs of recent hemorrhage. There were tubercles in the upper lobes of both lungs. The heart was small and pale. The spleen was the size of a small cantaloup, it was firm and contained one large grayish white nodule. Both of the testes contained numerous nodules. The inner surface of the left temporal bone contained nodular masses which were not attached to the dura. The distal portion of the left radius and that of the ulna showed extensive destruction immediately underneath tumor-like masses of the periosteum. The second toe of the right foot was similarly affected. Section of the peripheral nerves revealed no abnormalities.

Microscopic Studies—Sections from the following structures were stained with hematoxylin and eosin, Mallory's connective tissue stain and azure II and eosin.

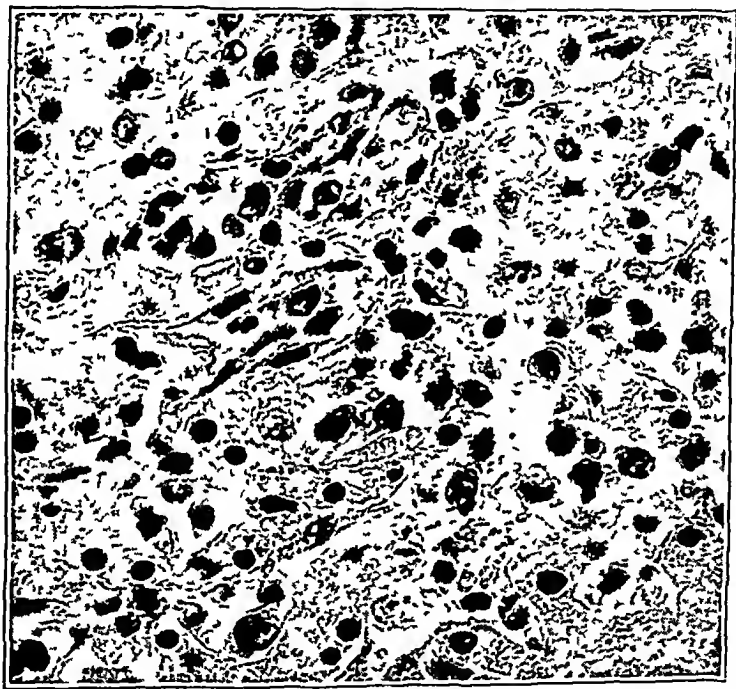


Fig 2—Section of liver showing monocytes in the sinuses and proliferation of Kupffer cells

lung, liver (two specimens), spleen (two specimens), lymph nodes (four specimens), periosteum (two specimens), bone (two specimens) and skin (three specimens)

Lung Only the picture of fibrocaceous tuberculosis was observed. The endothelioid cells were normal, i. e., the general reticulo-endothelioid state appeared to have had no modifying influence on these reactive cells against the tuberculous irritant.

Liver There was no fibrosis, nor was there any important degeneration of the parenchymal cells. In the perilobular fibrous tissue there were occasional rather large infiltrations of small lymphocytes with a minor intermixture of monocytes. Most conspicuous was the fact that invariably monocytes were present in the sinusoids, they were most abundant at the centers of the lobules. There was no



Fig 3—Section of lymph node showing replacement of cortex by reticuloendothelial proliferation. Only a small island of normal lymphoid tissue remains.

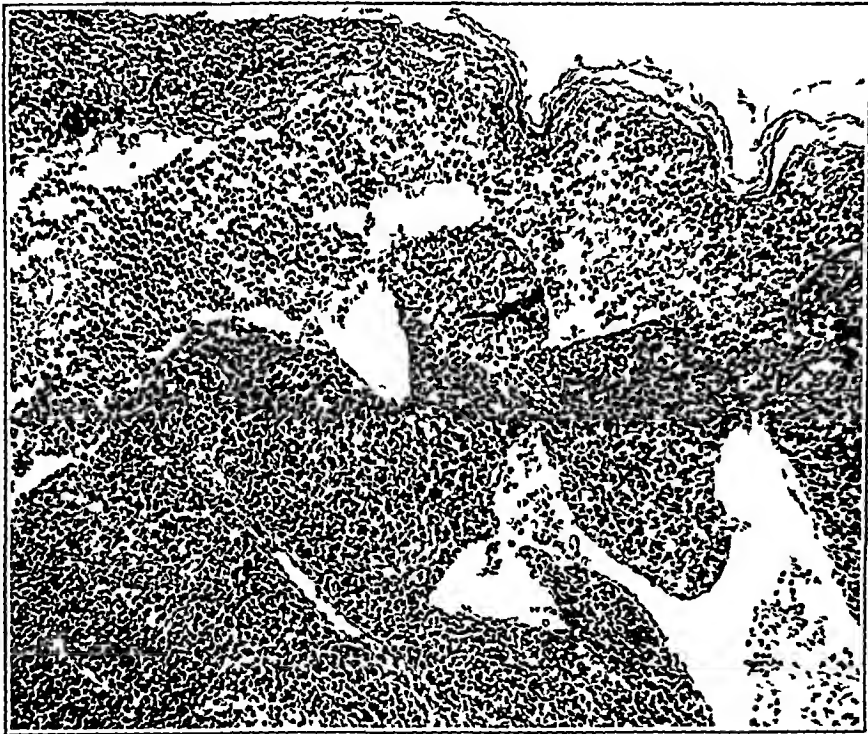


Fig 4—Section of lymph node showing cortical sinus crowded with monocytes. The reticulum between sinuses is expanded by proliferation into broad trabeculae.

question as to the identification as monocytes and macrophages, from which there was a clearcut transition to fixed Kupffer cells. There were large numbers of monocytes in some of the dilated portal veins, but in view of a large intermixture of hemosiderin granules it was considered possible that their presence was artefact, *i. e.*, due to postmortem "embolism" from the spleen.

Lymph Nodes In all the sections from the various regional lymph nodes the order of change was the same, consisting of a more or less diffuse reticulo-endothelial hyperplasia. In most sections monocytes dominated the picture. At times both the reticular and the monocytic features were exhibited in the same histologic section.

In the earlier stages of hyperplasia it was still possible to recognize the architecture of lymph nodes, thus, although the cortex may have been transformed into a broad, diffuse sheet of monocytes, the shadowy outlines of the cortical follicles could still be distinguished. In addition, the lymph sinuses could be clearly discerned, they were filled with monocytes and granular debris. Such positions were particularly valuable for differentiating against a sarcomatous process because the endothelial lining was so frequently preserved over long stretches, even though the ordinarily delicate strand of stroma between them had been transformed into heavy trabeculae as the result of the monocytic hyperplasia. In short, it is believed that if the process had been sarcomatous the normal architecture would have been disrupted in the presence of such a high grade of cellular hyperplasia. One of the peribronchial lymph nodes was of hemolymph type throughout, and in another node of unknown regional origin there was a definite island of such tissue within the capsule.

In other nodes the architecture was completely destroyed. There was a delicate reticular fibrillar stroma, on which the cells were largely spindle shaped or stellate, although smaller or larger areas of free monocytes were interspersed from place to place. It appears thus that monocytes dominated the picture at the earlier and reticulocytes predominated in the later stages of the disease.

As to cytologic details, the cytoplasm was uniformly larger than that of the lymphoid cell, it stained a light basophilic hue with azure II and eosin and at times exhibited dendritic polar processes, which could be followed up into close relationship to reticular fibrillae, as demonstrated by the Mallory aniline blue stain. Where the cytoplasm was relatively bulky it was finely vacuolated, and some cells contained granular debris and fragments of erythrocytes, which indicated phagocytic properties. Their nuclei were larger and more vesicular than those of lymphocytes and had a clearcut perinuclear membrane and a delicate spongy chromatin structure. Nucleoli were often absent or ill defined, although some cells contained from one to three distinct small round to stellate chromatin bodies. Mitotic figures averaged 2 per high power field, many nuclei were indented, and some were folded, the latter variations from the usual round to oval shapes were noted especially in the loosely arranged, relatively free cells. A definite genetic relationship between cells within the sinus and those lining it was established, the phagocytic quality of the cells was best demonstrated within sinuses. These cytologic studies were particularly valuable in differentiating the condition from Hodgkin's or Sternberg's disease because the proliferating cell types were so pure, *i. e.*, reticular and sinus endothelial cells.

Spleen The large nodule which occurred in this organ had the same structure as that described for the lymph nodes, *i. e.*, the normal architecture was destroyed except for persisting trabeculae and an occasional shadowy splenic nodule or sinus. There was a tendency toward early stages of sclerosis. In parts of the spleen not involved by the nodule the general architecture was still fairly well

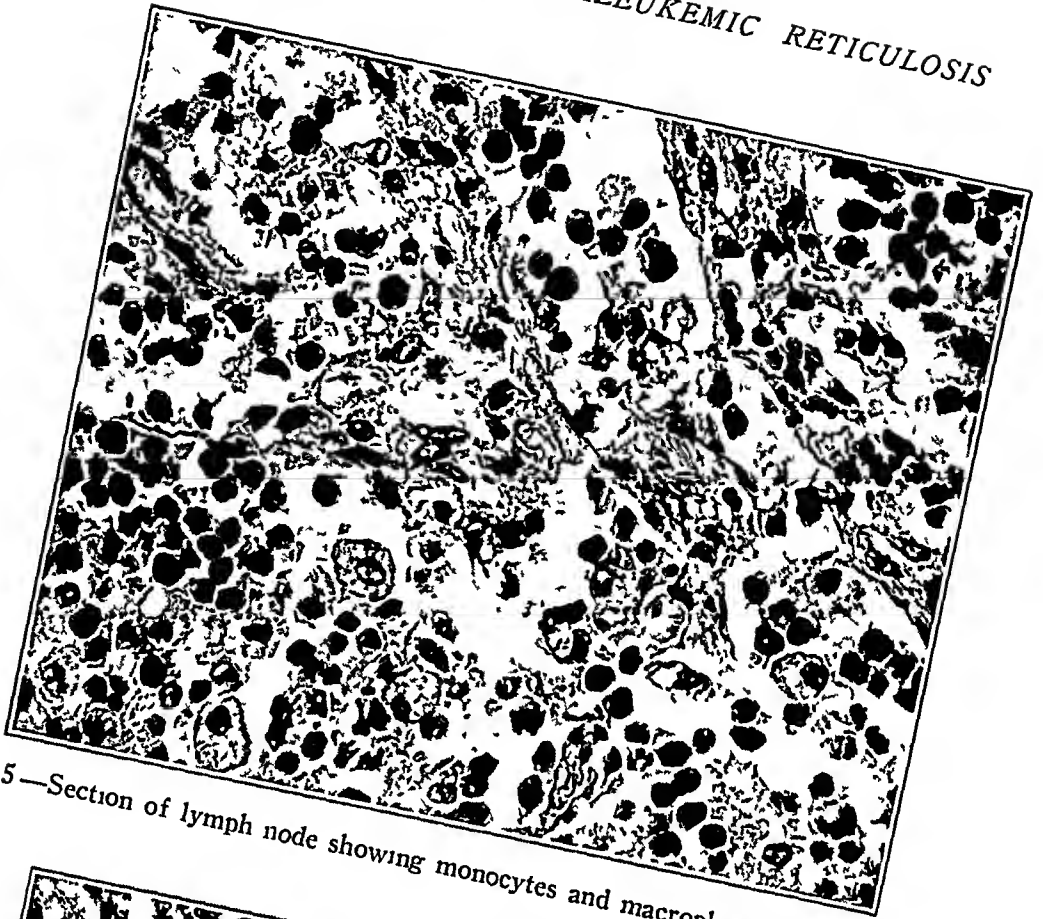


Fig 5—Section of lymph node showing monocytes and macrophages in sinuses

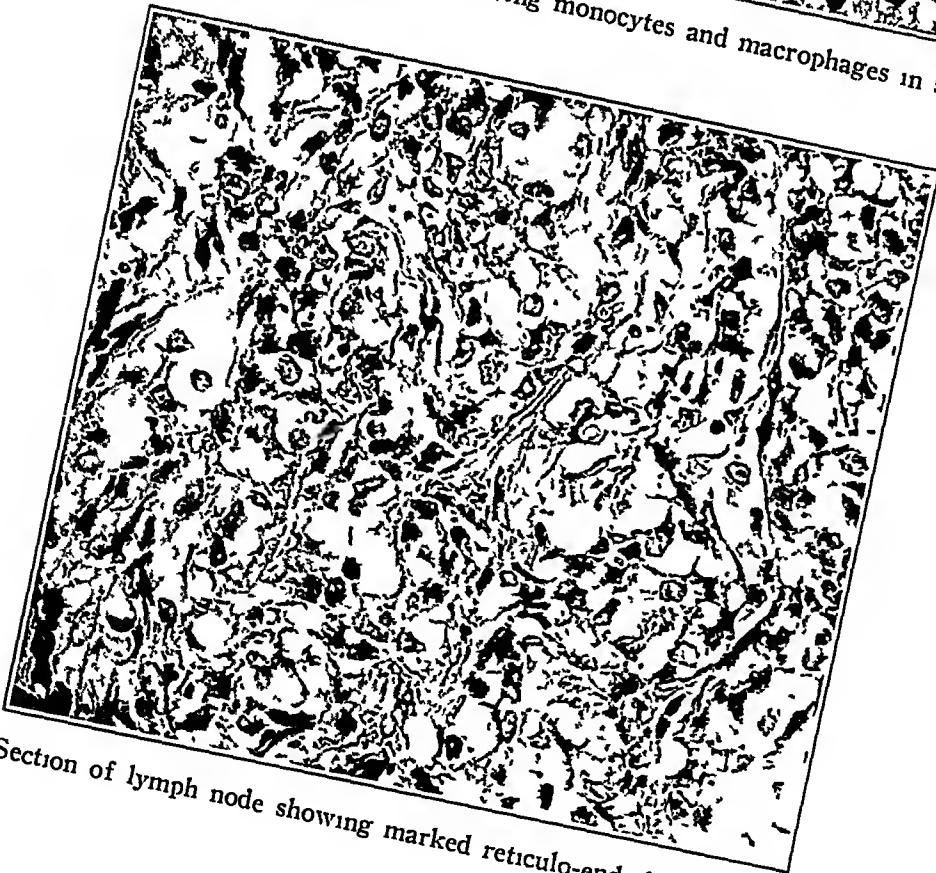


Fig 6—Section of lymph node showing marked reticulo-endothelial hyperplasia

preserved. However, the splenic nodes were poor in cells, and the sinusoids were crowded with monocytes and endothelial cells. Here again transition between cells of the reticulum and those of the sinuses was clearcut.

Bone The periosteum was massively thickened or replaced by diffuse infiltrations of monocytes and reticular cells. The marrow spaces were hugely dilated by the same types of cell. Hematopoietic cells could not be identified, being replaced by a loose fibrillar stroma supporting irregular accumulations of the monocytic cells. The cortex of the bone was partially destroyed, scattered remnants of broken-down trabeculae remaining in the degenerated masses of cells. The subcortical cancellous bone was sparsely trabeculated, the trabeculae being rather bulky and occasionally exhibiting zones of proliferating osteoblasts at their borders.

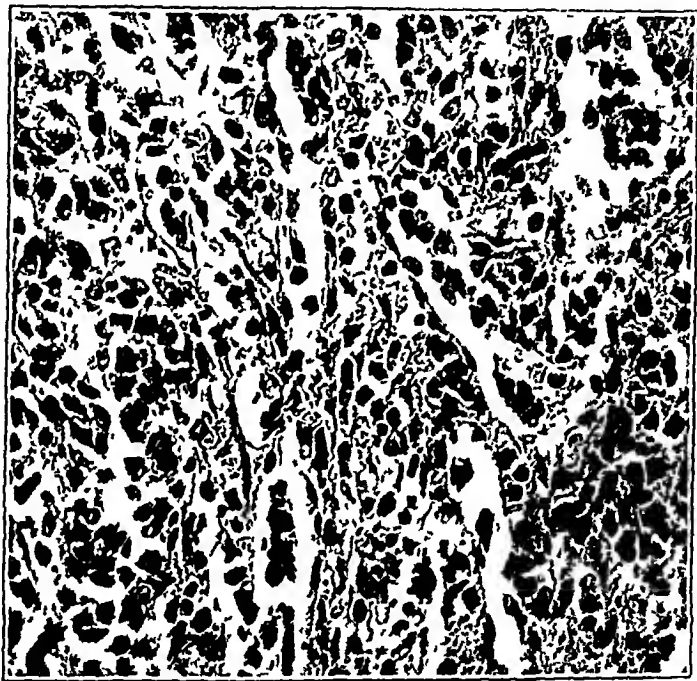


Fig 7—Section of spleen showing hyperplasia of sinus endothelium as well as of cells of the reticulum similar to the changes in the lymph node

Skin The epiderm was essentially normal. In the corium the heaviest infiltrations occurred in the deepest parts. They were essentially diffuse, the only suggestions of localization occurring around the hair follicles. At one place the tissue consisted entirely of broad areas of infiltrating cells within which a few islands of collagenous material were enclosed. In positions less extensively involved the cells occurred as chains which surrounded the collagen bundles so uniformly as to produce a mosaic appearance. In other parts there was a definite tendency for such closely placed strands to extend parallel to the cutaneous surface.

As to the type of cell concerned, monocytes predominated, being most conspicuous in the more massive infiltrates of the deeper parts of the corium and subcutaneous tissue. The reticular arrangements also occurred in masses, and it was in these that the aforementioned parallel strands occurred.

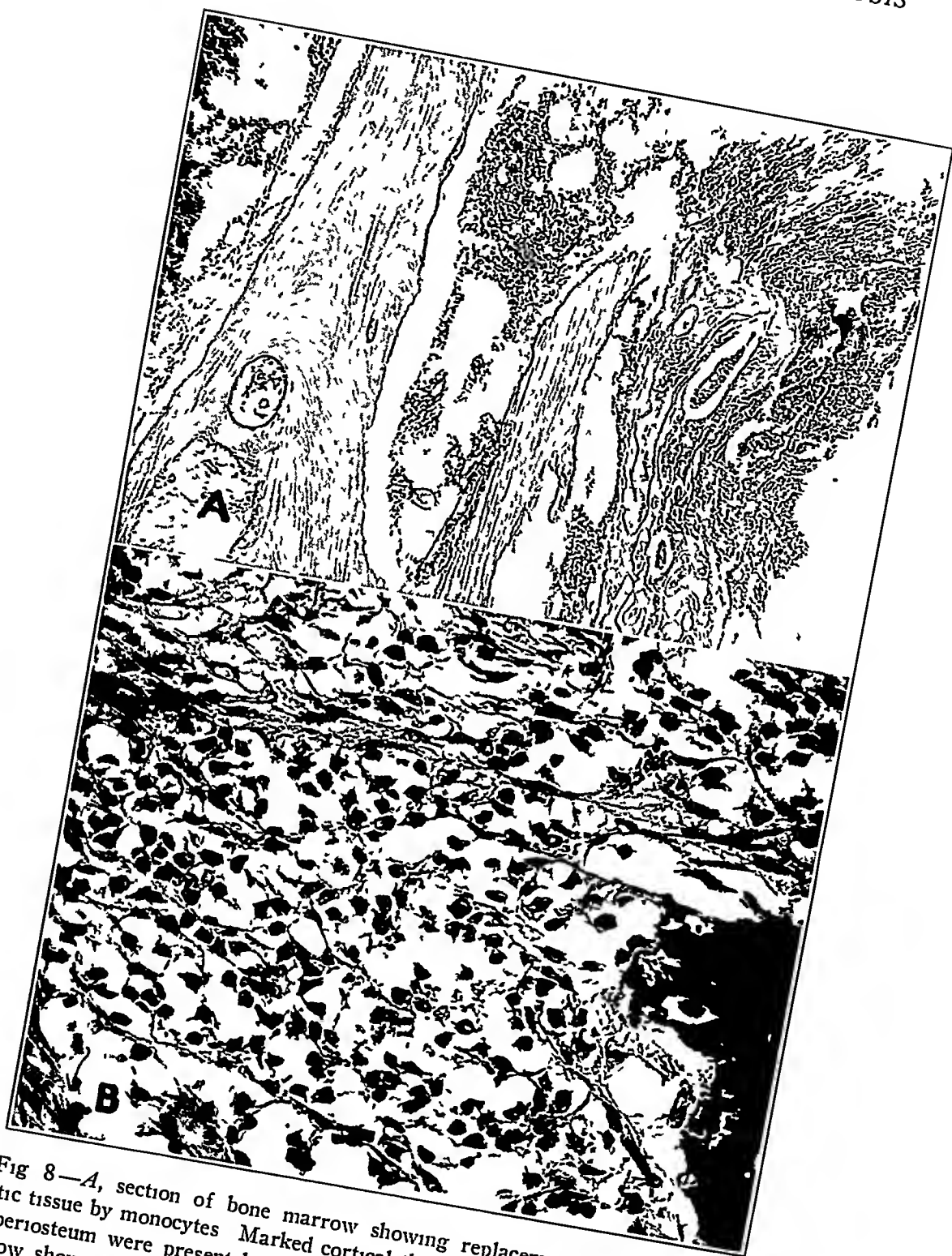


Fig 8—*A*, section of bone marrow showing replacement of normal hematopoietic tissue by monocytes. Marked cortical thinning and erosion and infiltration of the periosteum were present but are not visible in the section. *B*, section of bone marrow showing reticulosis.

The uppermost parts of the corium, while notably infiltrated, were inconspicuous in this respect in comparison to the deeper parts. The pars papillaris was not involved. In the subpapillary region the cells approached more the size of the lymphocyte, although larger monocytic cells were frequently identified as such, particularly when they occurred as more or less cylindric masses in the lymph spaces.

There was one mass of sharply circumscribed cells, measuring 10 by 4 mm, which was so sharply separated from the skin proper that it clearly indicated an independent subcutaneous nodule. In sections studied it did not appear to have any connection with the dermal infiltrate.

Summary of Histologic Observations—The most massive involvement occurred in the lymph nodes, skin, bone marrow and spleen. The order of change was

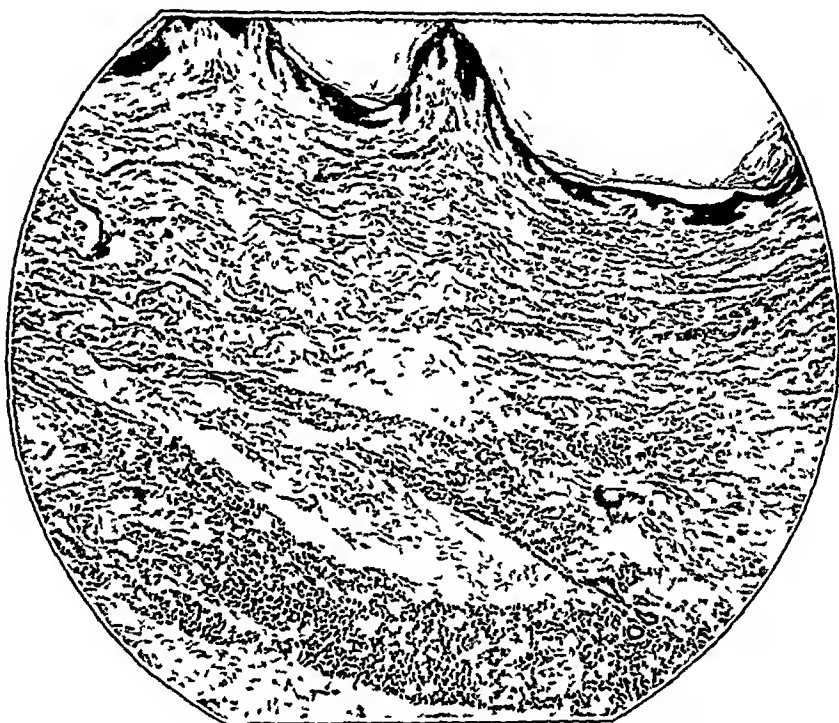


Fig 9—Section showing location of infiltration deep in the skin

the same in all, consisting of such extensive infiltrations of monocytes and stellate and spindle cells that the normal architecture was greatly destroyed. The affinities of such cells were established, we believe, with the reticulo-endothelial system (1) because blood-forming tissues were the ones outstandingly affected and (2) because the types of cells concerned could be referred to that system by appropriate staining methods. In the latter connection phenomena observed in the spleen and liver were of particular value because they established relationships between fixed cells of reticulo-endothelium and the free ones in the sinuses.

Histologic Diagnosis—The diagnosis based on histologic observations was diffuse reticulo-endotheliosis affecting the lymph nodes, spleen, bone marrow, liver and skin and fibrocaceous tuberculosis of the lungs.

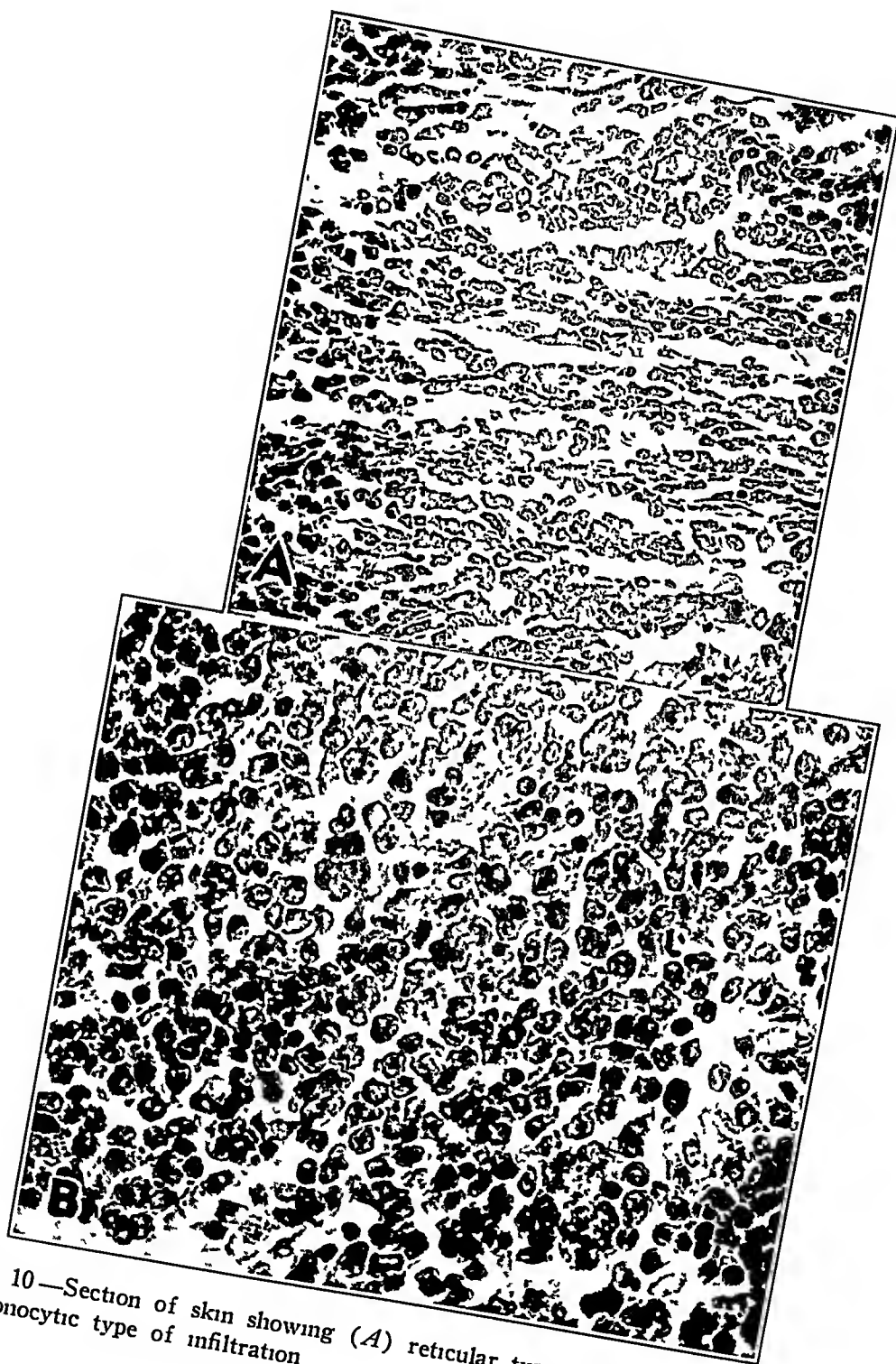


Fig 10—Section of skin showing (A) reticular type of infiltration and (B) free monocytyc type of infiltration

CLASSIFICATION

In the beginning, Warthin included thirty-two cases of granuloma fungoides among his five hundred and six cases of lymphoblastoma. He classified the disorder as follows

	No of Cases
Aleukemic lymphoblastoma	23
Aleukemic lymphoblastoma becoming leukemic	5
Aleukemic myeloblastoma	1
Leukemia cutis	3

This is sufficient to indicate that it was his intention to classify certain types of lymphoblastoma when they occurred on the skin with the clinical entity known as granuloma fungoides. He regarded all the lymphoblastomas as neoplastic, subsequently this thesis has been criticized (Ewing,⁸ Krumbhaar¹⁰), but it is not within the purview of this paper to enter into the interminable ramifications involved in the classification. Suffice it to say that as things stand today the general term cutaneous lymphoblastoma has become established among dermatologists as a convenient clinical designation to cover granuloma fungoides-like entities up to the point where more exhaustive studies become sufficient to indicate some definite relationship of the cutaneous condition to internal body processes. That is, we believe that the term cutaneous lymphoblastoma by virtue of usage is a useful, although only temporary, designation and that it should be retained until "cell type" nomenclature becomes stabilized. It should not connote any particular pathologic process. Just as soon, however, as a particular disorder can be classified according to a particular involvement of blood-forming tissue the term should be replaced by a more accurate one couched in terms of hemocytology.

A rather complete catalog of such conditions has been compiled¹¹. Suffice it to say for the present that theoretically there are twenty-two such disorders, of which thirteen have been thus far recorded which exhibit cutaneous expressions of one kind or another. Some of the thirteen disorders have been recorded but once or twice, the ones most commonly met are already well known to dermatologists, namely, Hodgkin's disease, granuloma fungoides, leukemic lymphadenosis and aleukemic lymphadenosis. In how far the cutaneous features can be

8 Ewing, James, cited by Krumbhaar¹⁰

9 Footnote deleted by author

10 Krumbhaar, E. B. The Lymphomatoid Diseases, *J. A. M. A.* 106:286 (Jan 25) 1936

11 Weidman, Fred D., and Custer, R. P. The Scope of the So-Called "Cutaneous Lymphoblastomas" in Relation to Lesions of the Haematopoietic System, *Proc. Internat. Dermat. Cong.* 2:91 (Sept) 1935

reconciled with granuloma fungoides remains to be ascertained. But in any event it must be admitted that it is constructive to add other diseases to the list even though they occur rarely.

Differential Diagnosis—In our case Hodgkin's disease may be eliminated not so much on clinical as on histologic grounds. While the degree of fibrosis was suggestive, Dorothy Reed cells were not observed. The purity of the cell type already mentioned is decisive. Reticulum cell sarcoma (including Hodgkin's sarcoma) may be similarly eliminated because in the extensive examinations of tissue the histologic picture of that condition was not observed.

Lymphosarcoma and leukosarcoma may be eliminated because a primary focus did not exist, again, the precise cytologic studies already emphasized remove these possibilities. As to granuloma fungoides, we have already indicated that we have no objection to this designation so far as the cutaneous aspects are concerned, we prefer to go farther, however, and aim at a diagnosis which will connote the entire biologic situation.

COMMENT

In our case there was a preliminary itchy diffuse dermatitis lasting five months, after a remission resulting from treatment it recurred in a modified form in four months. Symptoms of pulmonary tuberculosis were recognized at the eleventh month. At the twelfth month a non-pruritic dermatitis developed. At the thirteenth month a moderate adenopathy and splenomegaly were detected. The tumor stage developed at the thirteenth month, after which the remaining course of the disease (nine weeks) was fulminating, consisting of marked emaciation, fever, severe symptoms in the joints and death.

The roentgen studies were valuable in that they demonstrated disease in the bone marrow with infiltration and destruction of bone—a point which may be of some diagnostic value in cases of similar disorders in the future. These observations were confirmed at necropsy, after which microscopic examination of tissue referred the proliferative processes to the reticulo-endothelial system. Since there was no leukocytosis at any time, the disorder may be classified as an aleukemic reticulosis.

With two important exceptions this disorder closely parallels the leukemic reticulosis (monocytic leukemia) studied by Mercer and by Loveman—the clinical course was rapidly fatal, the adenopathy was not extreme and the cytologic picture was similar. It may be of significance as pointing to the reticulo-endothelial system that the lesions were dusky or bluish red, this remains to be determined as a generality. By contrast with leukemic reticulosis, the disorder in our case produced lesions of the order of tumors and did not produce a leukocytosis.

SUMMARY

A widely generalized dermatosis affecting a Filipino in Hawaii passed through a premycotic and a tumor stage. The course was fulminating, covering only fifteen months. At necropsy extensive tumor-like infiltration of all the blood-forming tissues was found. Histologic examination referred the proliferation to the reticulo-endothelial system. As leukocytosis did not occur, the disorder must be regarded as aleukemic reticulosis to which were added cutaneous expressions of the order met in the lymphoblastomas.

Since the cutaneous features were regarded in Hawaii variously as those of leprosy or of Hodgkin's disease and since the cutaneous course paralleled that of the lymphoblastomas, the importance of studies of the lymph nodes and bone marrow are obvious in establishing the diagnosis. It is therefore urged that in future cases of lymphoblastoma biopsies on bone marrow from the sternum be made.

It is evident that in this case aleukemic reticulosis reproduced the clinical symptoms and course of the lymphoblastomas. As the original scope of the lymphoblastomas, as defined, did not clearly include the reticuloses, the condition in our case can be classified with the lymphoblastomas only by sufferance or until it is definitely known that Kern and Waithm intended to assign a wider scope to their concept of lymphoblastoma. In any event, rather than attempt the construction of a new pathologic entity which would accommodate the disorder exhibited by our patient as well as other diseases of blood-forming tissue characterized by the presence of cells of a particular type, we deem it wise to place it tentatively in the group of the lymphoblastomas, or, better, in that of the "lymphomatoid diseases" as defined by Krumbhaar.¹⁰ Dermatologists must await a sufficient accumulation of cases and the results of exhaustive studies of blood-forming tissues with attention to cell types before attempting the final analysis, generalization and classification which would lead to a logical nomenclature for the mycosis fungoides-like dermatoses which are associated with disease of blood-forming tissue. Cases of such disorders cannot be discovered without a searching study of the cell type concerned according to the methods of hemocytologists, in which biopsies on marrow from the sternum as described by Custer¹² promise most help to the clinician.

ABSTRACT OF DISCUSSION

DR A. B. LOVEMAN, Louisville, Ky. There is a great deal of controversy concerning the actual existence of monocytic leukemia because of the diversity of opinion regarding the origin of the monocyte. Drs. Wayson, Weidman and

¹² Custer, R. P. Studies on the Structure and Function of Bone Marrow, *Am J M Sc* 185 617 (May) 1933.

Lynch apparently favor the theory of reticulo-endothelial origin at least in part Monocytic leukemia (Schilling type) may be considered a pathologic condition in which there is extensive hyperplasia of the reticulo-endothelial tissues associated with the appearance in the peripheral blood of abnormal cells of the monocytic series

The condition of the patient of Dr Wayson and Dr Weidman certainly resembled mycosis fungoides clinically Pathologically there was an extensive reticulosis or reticulo-endotheliosis The fact that there were no abnormal white cells in the peripheral blood further classifies the disorder as aleukemic reticulosis or aleukemic reticulo-endotheliosis Had the peripheral blood revealed extensive invasion of immature and abnormal cells of the monocytic series, the condition would have qualified as monocytic leukemia The invasion of the blood stream by these cells does not alter the fundamental pathologic process In fact, the authors stated that the condition in their case practically paralleled that in previously reported cases of leukemic reticulosis (monocytic leukemia) with the exceptions that their patient had no changes in the peripheral blood and that cutaneous tumors were present

One of the most interesting features in this case is the invasion of the osseous tissue It is quite likely that in the future the recognition of such involvement by roentgen examination may prove to be of great diagnostic significance

I concur heartily with Drs Wayson and Weidman in their opinion that both leukemic and aleukemic reticulosis should be admitted to the group of lymphoblastomas

Dr Lynch has performed a gigantic task in his attempt to differentiate monocytic leukemia (leukemic reticulosis) from aleukemic reticulosis on clinical and histologic grounds Heretofore I have regarded such a differentiation as impossible, and I still favor the view that the two conditions are fundamentally the same except that one is associated with extensive abnormality in the peripheral blood whereas the other is not

Dr Lynch stated that some authors prefer to consider monocytic leukemia in its aleukemic form and aleukemic reticulo-endotheliosis as the same disease I do not share this opinion, because aleukemic reticulo-endotheliosis implies, as Dr Wayson and Dr Weidman stated, a reticulosis with no appearance of abnormal cells in the blood stream, whereas an aleukemic state of monocytic leukemia implies at least some qualitative changes in the blood, although the white blood cell count may not exceed the normal limit

There is some doubt in my mind as to the exact classification of the disorder in several of Dr Lynch's cases Case 1 is undoubtedly one of reticulosis, but without knowledge of the hematologic data it is difficult to classify it as one of leukemic reticulosis Two additional cases were reported as examples of aleukemic reticulo-endotheliosis In the one (case 6) there was an abnormally high white blood cell count with only 10 per cent mature white cells, in the other (case 7) there were 65 per cent atypical mononuclear cells although the total count was only 4,000 white cells per cubic centimeter In both of these cases there was rather extensive monocytic infiltration of the skin It is difficult to rule out monocytic leukemia in these cases—in case 7, however, the disorder was in its aleukemic phase

It is questionable whether the cutaneous manifestations were sufficiently characteristic to be diagnostic or pathognomonic per se This is well illustrated when one compares the similar pathologic features in the case of Dr Wayson and Dr. Weidman and those in some of Dr Lynch's cases and yet observes the great divergence in the cutaneous manifestations As leukemic and aleukemic reticulosis become better recognized, a diversity of cutaneous manifestations will undoubtedly be noted

The cutaneous necrosis noted in several cases may well be the result of marked diminution or of absence of polymorphonuclear cells in the blood stream. I have seen similar lesions associated with agranulocytosis, granulocytopenia and aplastic anemia—the diseases, incidentally, which are sometimes difficult to differentiate from the aleukemic phase of monocytic leukemia.

Both of these papers were well presented and should prove thought stimulating to the dermatologist. They show clearly that correlation of the clinical, hematologic and histologic features is necessary to establish a specific diagnosis. Future progress will depend more on the accurate recognition of the cell type than on any other single factor.

DR ARTHUR W STILLIANS, Chicago. I wish to mention a case of monocytic leukemia presented before the Chicago Dermatological Society some years ago. The patient at one time had a white blood cell count of 23,000 and from 50 to 71 per cent monocytes. There was a generalized exfoliative condition associated with infiltration of the skin and many distinct, sharply defined papules.

Histologic studies showed no specific infiltration, but, as has been stated, it may be that a specimen taken later would have given different results.

The patient was 70 years old and derived much benefit from roentgen treatment. She died a couple of years later of pneumonia.

DR HAMILTON MONTGOMERY, Rochester, Minn. It is important to differentiate between the Naegeli and the Schilling type of monocytic leukemia. In both there is indentation of the nuclei to a certain extent, and the two conditions can be differentiated only by careful hemocytologic studies. I do not believe that they can be differentiated on the basis of the histologic picture in sections of the skin alone. Hemocytologists do not agree regarding the origin of all the white cells. Some maintain that the reticulo-endothelial cells and the monocytes can also give rise to lymphocytes, thus linking the reticulo-endothelial diseases with the lymphoblastomas. I therefore believe that the term lymphoblastoma is as good a one as can be used for the time being.

Two cases of monocytic leukemia of the Naegeli type were observed at the Mayo Clinic. In one of these the disorder started with generalized erythroderma, mycosis fungoides-like plaques and the histopathologic picture of a nonspecific lymphoblastoma. Only after four years, shortly before the patient's death, did the hemocytologic examination give positive results and show a Naegeli type of monocytic leukemia, with 40 per cent monocytes. The condition in this case probably represented the autochthonous development of a lymphoblastoma which in the beginning was mycosis fungoides and terminated as a Naegeli type of leukemia.

In the other case changes in the blood appeared first and cutaneous manifestations consisting of nodules and necrosis developed only in the terminal phases.

Mycosis fungoides, as Fraser has emphasized, is accompanied by marked changes in the reticulo-endothelial cells of the skin, and there may be a certain number of immature monocytes as well as immature forms. It is important to correlate all the various diagnostic measures in order to arrive at a correct diagnosis in cases of monocytic leukemia or of any of the lymphoblastomas.

DR. D W GOLDSTEIN, Fort Smith, Ark. Recently I have observed a case of monocytic leukemia in a woman aged 58 who was referred to me because of a purpuric lesion on the cheek which resembled a streptococcic blister. There was no localized erythema or swelling around the lesion. The patient's temperature was 101 F. There were no palpable glands or enlargement of the spleen. Examination of the oral cavity disclosed an ulcer on the gingival surface at the second bicuspid tooth. This lesion had previously been cauterized. A purpuric lesion

was found on the posterior wall of the pharynx. A blood count showed 88,000 white cells and numerous other cells which were considered to be monocytes. A tentative diagnosis of monocytic leukemia was made. Several days later the total white cell count was 150,000, and there was an increase in the number of monocytes. Ulcerative gingivitis developed during the next few days. There was also an increase of the number of white blood cells and in that of monocytes. The patient was sent to the hospital for transfusion five days after the diagnosis was made, but she died suddenly two hours after entering the hospital. Permission for autopsy was refused. Slides were sent to the Simpson Memorial Institute, Ann Arbor, Mich., where the diagnosis of monocytic leukemia was confirmed.

DR M G BOHRD, Peoria, Ill. Dr Weidman mentioned the necessity for a broader name to include the whole group of diseases under consideration. Evidently unless one believes that the monocyte and the lymphocyte have interrelations and can be formed one from the other, this group of diseases does not belong to the lymphoblastomas, and certainly the name lymphoblastoma cannot be applied to the specific cutaneous lesions associated with the myelogenous types of leukemia.

In pathology the whole group of diseases due to marked proliferation of the cells of the circulating blood and of their precursors does have a name, and I think that this name could be applied to the special manifestations under consideration. Since the whole group of white cells—monocytes, lymphocytes and granulocytes—are called leukocytes, the name given to all these neoplastic or pseudoneoplastic diseases is leukoses. The simple name cutaneous leukoses could be adopted, for the cutaneous manifestations, and that would cover the entire group.

DR FRED D WEIDMAN, Philadelphia. It has been brought out by a number of the discussers that controversy about terminology still runs riot among hematologists. That is one more reason for dermatologists to refrain from trying to adapt dermatologic nomenclature too strictly to hematologic nomenclature. One should let the hematologists fight out the question among themselves. When they have stabilized their nomenclature it will be possible for dermatologists to multiply the dermatologic nomenclature.

The general practicing dermatologist wishes to know how he can help the hematologist in the finer cytologic studies of these conditions. 1 He should take numerous, at least a dozen, samples of blood. The hematologist has to employ various stains. It may be necessary to make the oxidase test and to use Mallory's connective tissue stain and other stains. 2 He should secure a sample of bone marrow, if possible. Dr Custer has published the technic for securing biopsy material from the bone marrow of the sternum. He does it often at the Philadelphia Hospital, and thus far the procedure has never caused osteomyelitis. 3 The dermatologist should have roentgenograms made. It is obvious that where there is involvement of the marrow and bones, this is a logical avenue to turn to.

In some of Dr Lynch's cases the disorders were suggestive because they had a bearing on etiology. In the first cases that he reported the disorder started as what appeared to be an infection and the course was fulminating. If these cases are to be accepted as instances of disease of blood-forming tissue—classified as leukemia—it appears that some types of leukemia at least have an acute infectious causation, which is pertinent to the controversy whether the lymphoblastomas are neoplastic or not. Warthin and the Michigan school in general contend emphatically that the lymphoblastomas and Hodgkin's disease are neoplastic conditions.

DR FRANCIS W LYNCH, St Paul, Minn. Dr Montgomery mentioned the reticulo-endothelial origin of lymphocytes. Although it was not indicated on the

lantern slide, Downey agrees that some lymphocytes develop directly from reticulo-endothelial cells, but the majority develop in lymphoid tissue by the division of apparently mature lymphocytes

Dr Loveman brought up a number of points which deserve comment. First of all, I apparently did not make clear my opinion of the relation between monocytic leukemia and reticulo-endotheliosis. I believe that the Naegeli type of monocytic leukemia must be differentiated from reticulo-endotheliosis and that the two conditions have nothing in common. The Naegeli type of monocytic leukemia is a mixed form of myelogenous leukemia. I think that there are no essential differences between monocytic leukemia of the Schilling type and "primary" reticulo-endotheliosis.

Dr Loveman rightly questions the classification of the disorder in case 6, in which the white blood cell count was 38,000 and there was a papular eruption on the neck. That is gone into in more detail in the paper. The youth with the chronic ulceration (case 8) presented an interesting blood picture. His white cell counts were within normal limits, but the proportion of the different cells varied considerably. Most often the counts showed that 65 per cent of the cells were lymphocytes, but a few days later as many as 65 per cent would be polymorphonuclear leukocytes, that alternation was repeated several times in the course of the disease.

I am not sure that the understanding of aleukemic leukemia is clear. Is it necessary that qualitative changes in the constituents of the white blood cells be present? May not the white blood cell be entirely normal, showing neither qualitative nor quantitative differences, and yet pathologic changes due to aleukemia be present in the tissues? It is my opinion that this is not uncommon in aleukemic lymphatic leukemia.

CUTANEOUS LESIONS ASSOCIATED WITH MONOCYTIC LEUKEMIA AND RETICULO-ENDOTHELIOSIS

FRANCIS W LYNCH

ST PAUL

Since the general knowledge of lymphatic and myelogenous leukemia was greatly advanced by a study of the cutaneous lesions of these conditions, it is unfortunate that dermatologists have only recently become interested in monocytic leukemia. This condition was first described in 1913 by Reschad and Schilling-Torgau,¹ who reported a case of this disease involving the skin observed in Arning's clinic. Monocytic leukemia is characterized by an increase of monocytes in the blood but is indistinguishable clinically from the other leukemias. Both specific and nonspecific cutaneous lesions are commonly associated with this disease.

Reticulo-endotheliosis has also been the subject of much study by hematologists, but the recent advances in the hematologic aspect of this condition have not received sufficient attention in dermatologic literature. Among dermatologists there has developed a tendency to place all atypical pathologic processes involving the hematopoietic and lymphatic tissues in a large ill defined group and to call them all lymphoblastoma.

When Mallory in 1914 introduced the term lymphoblastoma he referred only to the diseases involving tissues and cells of lymphoid nature. Myeloid and monocytic leukemia, reticulo-endotheliosis and established mycosis fungoides should not be included under this title until more definite knowledge as to the development of the various blood and tissue cells is available.

It has been my privilege to observe a number of cases of monocytic leukemia and reticulo-endotheliosis in the various services at the University Hospitals. I shall discuss the clinical and the microscopic manifestations observed in these cases and attempt to show the relationship between these conditions and the other better known diseases of the hematopoietic system. It is hoped that the differentiations will be of

From the Division of Dermatology, University of Minnesota, Dr H E Michelson, Director

Read before the Section on Dermatology and Syphilology at the Eighty-Seventh Annual Session of the American Medical Association, Kansas City, Mo., May 13, 1936

1 Reschad, H., and Schilling-Torgau, V. Ueber eine neue Leukämie durch echte Uebergangsformen und ihre Bedeutung für die Selbstständigkeit dieser Zellen, *München med Wchnschr* 60:1981, 1913

service to dermatologists in assisting them to diagnose conditions belonging to this confusing group of cutaneous diseases

I shall not review the older theories of the development of blood cells as propounded by Maximov and by Naegeli. These theories have been modified more recently, but they are still not acceptable to a large group of hematologists. All agree that the mesenchymal syncytium in embryonal life gives rise to all the various blood cells. Downey² and many other hematologists believe that cells of the reticulo-endothelial system, which are direct descendants of this syncytium, retain their hematopoietic ability, which may later become manifest in a leukemic state by producing cells of the lymphoid, myeloid or monocytic series. Normally, however, the reticulo-endothelial system is active chiefly in the production of monocytes. Lymphocytes develop in lymphoid tissues almost exclusively by the division of apparently mature lymphocytes, while polymorphonuclear granulocytes develop from immature cells of the myeloblastic series in myeloid tissue.

Monocytes observed in leukemic blood may develop in either of two ways: (1) directly from the reticulo-endothelial system in a manner related to the normal or (2) in myeloid tissue as a development from the myeloblast. Thus two distinct types of monocytic leukemia have been described. In the first there is reticulo-endothelial hyperplasia with mobilization of the cells into the blood and differentiation to monocytes (Schilling type). In the second type the pathologic picture in the tissues is that of myelogenous leukemia, while myeloblasts and other immature granulocytes as well as immature and mature monocytes are present in the blood (Naegeli type).

MONOCYTIC LEUKEMIA

Monocytic leukemia is characterized by an increase in the number of monocytes of the blood. These cells are always present in normal blood but are much less numerous than lymphocytes or granulocytes. They are larger than large lymphocytes and have an abundant weakly basophilic cytoplasm, which is usually granular and frequently vacuolated. The eccentric nucleus is large and vesicular and may be oval, notched or lobulated. As mentioned previously, the monocytes of normal blood are produced by the reticulo-endothelial system. In true monocytic leukemia (Schilling type) the abnormal increase of immature monocytes results from an exaggeration of the normal process, that is, the immature cells are produced by the reticulo-endothelial system.

² Downey, H. Monocytic Leukemia and Leukemic Reticulo-Endotheliosis, in Bell, E. T. Textbook of Pathology, ed 2, Philadelphia, Lea & Febiger, 1934, personal communication to the author. Stasney, J., and Downey, H. Subacute Lymphatic Leukemia, *Am J Path* 11 113 (Jan) 1935.

The first patient reported to have monocytic leukemia¹ presented himself at Arning's clinic with a generalized macular eruption associated with stomatitis and nasal hemorrhages. The cutaneous changes consisted of infiltration with large mononuclear white blood cells. A great excess of monocytes was present in the blood.

Of the manifestations of monocytic leukemia, ulcerative gingivitis, petechiae and subcutaneous hemorrhages are the most common findings of interest to dermatologists. Of a series of cases reported by Doan and Wiseman³ cutaneous lesions were observed in about half.

Mercer⁴ in 1935 reviewed the literature on monocytic leukemia and reported two cases in which the cutaneous eruption was a prominent



Fig 1 (case 1) —Section from an early lesion of monocytic leukemia cutis, showing lymphoid and monocytoïd infiltration. Only two monocytes are pointed out but many more are present.

feature. He pointed out that two types of specific lesions are met: (1) red or brown macules and papules, which usually become blue later, and (2) pale shotty papules lying deeper in the skin; these lesions may develop into larger nodules.

Loveman⁵ has recently reported a case of monocytic leukemia in which specific cutaneous lesions were present. His description of the

3 Doan, C. A., and Wiseman, B. The Monocyte, Monocytosis and Monocytic Leukosis, *Ann Int Med* 8:383 (Oct) 1934.

4 Mercer, S. T. The Dermatoses of Monocytic Leukemia, *Arch Dermat & Syph* 31:615 (May) 1935.

5 Loveman, A. B. Monocytic Leukemia Cutis, *South M J* 29:357 (April) 1936.

histologic observations is particularly valuable and will be discussed later

Two further cases of monocytic leukemia with specific lesions are reported briefly

CASE 1—In a 67 year old man a penile lesion developed as a result of a chemical burn. Ulceration was followed by painful enlargement of the shaft and glans associated with weakness, chills and fever. Necrotic ulceration of the glans progressed in spite of local therapy. Numerous petechiae as large as 2 cm in diameter appeared over the entire body. There was also subconjunctival hemorrhage. A febrile course terminated with death five weeks after the onset of the initial symptoms. Microscopic study of the viscera at autopsy showed diffuse monocytic infiltration, sustaining a diagnosis of monocytic leukemia.

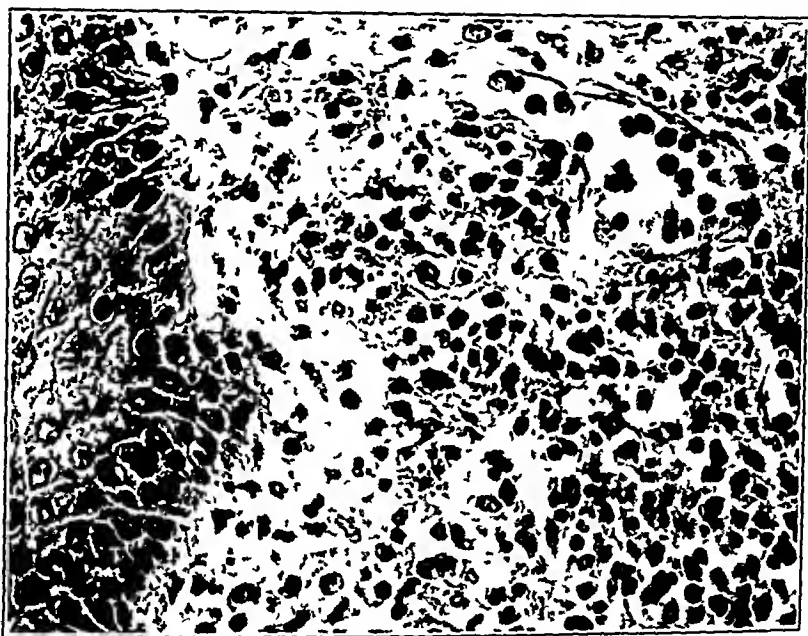


Fig 2 (case 1)—Section showing a later stage of the disease. There are looser structure, large reticular cells and numerous mature and immature monocytes characteristic of monocytic leukemia cutis.

In tissue removed before death a nonspecific change consisting of polymorphous infiltration and a loose supporting tissue was observed (fig 1). Sections of tissue removed at autopsy showed many polymorphonuclear leukocytes near the necrotic areas and a few large cells having a clear cytoplasm and a small dark eccentric nucleus. In the areas of diffuse infiltration there were mononuclear cells of various sizes, the smaller cells had round nuclei while the nuclei of many of the larger cells were oval (fig 2).

This case furnishes an example of the usual course, which progresses rapidly and simulates that of sepsis, even when the disease follows a more chronic course it usually terminates with similar acute symptoms.

The massive infiltration of the genitalia with progressive necrotic ulceration observed in this patient has not previously been described in association with monocytic leukemia

Naegeli Type of Monocytic Leukemia—As mentioned earlier, Naegeli has described a type of monocytic leukemia in which immature cells of both the myeloid and the monocytic series are observed. It is Downey's opinion that this disorder represents a form of myelogenous leukemia with hyperplasia of the myeloid tissues in which the myeloblast produces both granulocytes and monocytes.

In one of Montgomery's⁶ patients with the Naegeli type of monocytic leukemia the early cutaneous manifestations simulated mycosis fungoides.

CASE 2—A 58 year old woman had a white blood cell count of 144,000 and immaturity in all lines of polymorphonuclear cells. The diagnosis was mixed leukemia of the chronic monocytic myelogenous type. There were a number of noninflammatory infiltrated lesions on the arms and buttocks and an area of involvement on the leg which may have represented thrombophlebitis. At autopsy a diagnosis of chronic monocytic leukemia was made, but later microscopic study showed myeloid leukemic infiltration of the liver, spleen, kidneys and adrenal glands, and a final diagnosis of chronic myelogenous leukemia was made.

The upper portion of the cutis of an infiltrated lesion was practically free from the cellular infiltration which was rather uniformly diffuse throughout the remaining portions of the cutis. At the lower border were many immature cells, the proportion of lymphocytes increased near the surface of the skin. Many of the immature cells had oval or reniform nuclei, but most of the nuclei were round and slightly larger than those of the lymphocytes, the cytoplasm was eosinophilic and varied in amount.

The condition in case 2 represents the Naegeli type of leukemia and illustrates the difficulty encountered in properly classifying this disease. The cutaneous lesions were not particularly helpful in differentiating between the various types of leukemia, except that the presence of immature eosinophils suggested myelogenous leukemia, immature monocytes were also observed.

LEUKEMIC RETICULO-ENDOTHELIOSIS (EWALD)

In a small group of cases of leukemia one may demonstrate in the smears of blood unusual cells which resemble not only monocytes but also lymphocytes, myeloblasts, plasma cells and reticulo-endothelial cells.² Ewald described such a disorder as an instance of leukemic reticulo-endotheliosis, this nomenclature is unfortunate because many writers speak of monocytic leukemia as leukemic reticulo-endotheliosis. The exact relationship between these two diseases is not known.

6 Montgomery, H. Personal communication to the author.

In contrast with the observations in monocytic leukemia smears of blood from patients with Ewald's leukemic reticulo-endotheliosis show cells more primitive than the myeloblast. There is primary reticulo-endothelial hyperplasia plus increased hematopoietic function, the presence of immature monocytes differentiates this condition from the hyperplasia associated with sepsis which liberates only unaltered reticulo-endothelial cells or histiocytes. Leukemic reticulo-endotheliosis of the Ewald type is not common. It is regarded by some observers as a subleukemic form of monocytic leukemia.

The cutaneous changes observed in the following cases were non-specific and represent merely the hemorrhagic tendency so characteristic of all forms of leukemia. This feature, which is sometimes used as a differential point in distinguishing clinically between leukemia and lymphogranulomatosis, may provide some justification for grouping leukemic reticulo-endotheliosis with the true leukemias.

CASE 3—A 66 year old man exhibited the clinical and hematologic picture of chronic leukemic reticulo-endotheliosis. There were a number of petechiae in the scapular and clavicular regions and ecchymoses on the extremities. No other cutaneous lesions were observed. After four transfusions of blood the purpuric tendency disappeared.

CASE 4—A 51 year old man had the hematologic picture of leukemic reticulo-endotheliosis, with the reticular cells differentiated toward lymphocytes. He presented scattered petechiae, and later evidence of subcutaneous hemorrhages appeared on the trunk and extremities. There was also hemorrhage from the nose and mouth associated with a severe anemia.

Microscopic examination of one of the petechial areas did not show any change in the capillaries but disclosed only extravasation of red blood cells. There were no specific changes in the perivascular tissues.

ALBUKEMIC RETICULO-ENDOTHELIOSIS

The term reticulo-endothelial system has been used loosely to include nearly all the connective tissues of the body. Used in a strict sense it refers to the reticulum cells of the spleen and other lymphoid tissue as well as to the reticulo-endothelial cells of the lymph sinuses of the nodes and the blood sinuses of the spleen, liver, bone marrow, adrenal cortex and hypophysis. This system is composed of large mononuclear vacuolated cells capable of taking up granular material for storage.

Hyperplasia of the reticulo-endothelial system is a common response to infection and is evidence of the relation of this system to the development of immunity. In banal acute infections there is often sufficient response of this system to produce an increase of monocytes in the blood, occasionally in acute sepsis there is such active reticulo-endothelial response that unaltered reticulo-endothelial cells may be liberated into the blood stream. These observations correspond to the liberation into the blood stream of immature lymphocytes or granulocytes which frequently occurs in acute septic conditions.

Reticulo-endothelial hyperplasia is observed in certain chronic infectious diseases and in lymphogranulomatosis, granuloma fungoides and sarcoma of Kaposi. There is frequently an increase of monocytes in the blood and tissues in these diseases. The reticulo-endothelial system may also be involved in a lymphosarcomatous process, as pointed out by Fraser and Schwartz,⁷ who classified reticulo-endothelial disease with the lymphoblastomas because they believed that "the most constant anatomic function of the primitive reticular cells . . . is the production of the lymphatic series of cells." Observers who believe that the reticulo-endothelial cell is more active in producing monocytes than lymphocytes cannot place reticulo-endotheliosis with the lymphoblastomas as defined by Mallory.

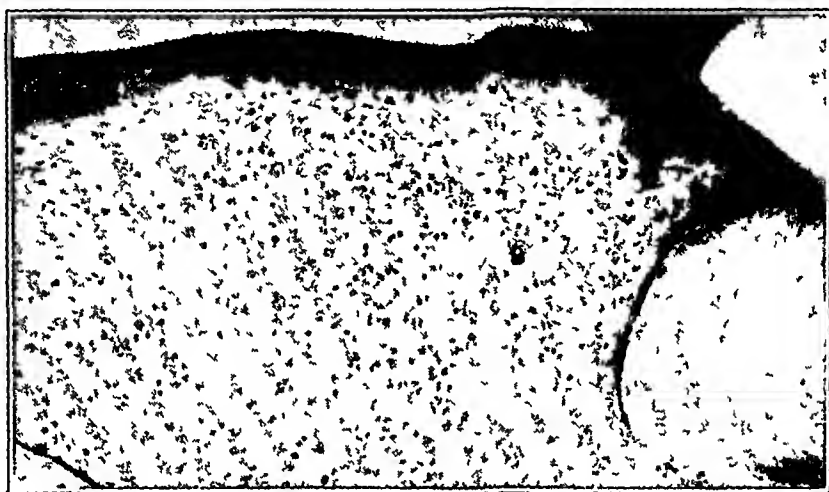


Fig 3 (case 5) —Generalized pustular eruption in an infant who died of acute reticulo-endotheliosis. The lesions were specific.

Hyperplasia of the reticulo-endothelial system associated with acute or chronic infectious processes or with the aforementioned granulomatous conditions is occasionally referred to as reticulo-endotheliosis. One must recognize that such reticulo-endothelial hyperplasia is secondary to the other process just as myeloid or lymphoid hyperplasia may be observed secondary to other diseases.

In lymphatic and myelogenous leukemia the hyperplasia of the lymphoid or myeloid tissue respectively is the essential feature of the disease, and aleukemic phases are observed with no changes demonstrable in smears of the blood. Since the hematopoietic tissue for monocytes consists chiefly of the reticulo-endothelial system, hyperplasia of this system should be the most striking feature of aleukemic monocytic leukemia. Because many confusing pathologic changes are observed in the reticulo-endothelial system and their exact relationships are not

⁷ Fraser, J. F., and Schwartz, H. J. Neoplastic Disease of the Reticulo-Endothelial System, *Arch Dermat & Syph* 33:1 (Jan) 1936.

absolutely known this condition is at present described as "reticulo-endotheliosis," although many observers regard it as the aleukemic manifestation of monocytic leukemia.

Aleukemic reticulo-endotheliosis may be acute⁸ or chronic⁹. The clinical course of the acute form is characterized by sudden onset, fever, necrotic angina and hemorrhagic diathesis—features which correspond to those of the other forms of acute leukemia and which recall Sternberg's opinion that acute leukemia is the result of sepsis. Although bacterial organisms have been observed in a few cases, in the majority they cannot be demonstrated, and most observers regard their presence as evidence of secondary invasion.

Chronic aleukemic reticulo-endothelial proliferation may be difficult to distinguish clinically and pathologically from the hyperplasia secondary to chronic infectious processes or lymphogranulomatosis, atypical forms may present a most confusing symptomatology and pathology. In spite of confusion as to the proper interpretation of the observations in some cases of these disorders there remains a group which most competent observers regard as chronic aleukemic reticulo-endotheliosis and which may well be called aleukemic monocytic leukemia.

The cutaneous lesions of reticulo-endotheliosis do not differ greatly from those of leukemia. In the acute forms one may observe macular or papular eruptions which seldom lead to the development of deeper nodules. There is a tendency to hemorrhage or necrosis in these lesions, and distinctly pustular eruptions may be observed, such as occurred in case 5.

8 Akiba, R. Ueber Wucherung der Retikulo-Endothelien und ihre Beziehung zu den leukämischen Erkrankungen, *Virchows Arch f path Anat* **260** 262, 1926. Morquio, L. Multiple Subcutaneous Neoplastic Tumors, *Arch Dermat & Syph* **31** 390 (March) 1935. Padvinec, E., and Terplan, K. Zur Frage der sogenannten akuten aleukämischen Retikuloze, *Arch f Kinderh* **93** 40, 1931. Sannicandro, G. Reticulo-endotheliosi leucemica con manifestazioni cutanee, *Haematologica* **15** 433, 1934. Klostermeyer, W. Ueber eine sogenannte aleukämische Retikuloze mit besonderer Beteiligung des Magen-Darm Kanales, *Beitr z path Anat u z allg Path* **93**.1, 1934. Sachs, F., and Wohlwill, F. Systemerkrankungen des reticulo-endothelialen Apparats und Lymphogranulomatose, *Virchows Arch f path Anat* **264** 640, 1927. Letterer, E. Aleukämische Retikuloze, *Frankfurt Ztschr f Path* **30** 377, 1924.

9 Goldschmid, E., and Isaac, S. Endothelhyperplasie als System-Erkrankung des hamatopoetischen Apparates, *Deutsches Arch f klin Med* **138** 291, 1922. Tschistowitsch, T., and Bykowa, O. Retikuloze als eine Systemerkrankung der blutbildenden Organe, *Virchows Arch f path Anat* **267** 91, 1928. Gery, L., Wolf, M., and Grevillod. Réticulo-granulomatoses, *Am J Cancer* **22** 243, 1934. Lauritzen, K. Ein Fall einer systemartigen Retikulumzellhyperplasie, *Virchows Arch f path Anat* **279** 603, 1931. Flarer, F. Cutaneous Endothelioma with Systemic Manifestations, *Arch Dermat & Syph* **31** 95 (Jan) 1935. Zentralbl f Haut- u Geschlechtskr **49** 154, 1934.

CASE 5—An eruption on the buttocks was noticed when the patient was 4 months old (fig 3) The lesions were macular and then became vesicular, they were followed by others appearing in the same region and then on the scalp, trunk and proximal portions of the extremities Two months later there was a generalized pustular eruption The white blood cell count was 15,000, and the differential count was normal An infection of the middle ear developed, and the cutaneous lesions became more severe, consisting of oval crusted shallow ulcers 0.5 cm in diameter There were numerous petechiae Study of the nodes, liver and spleen at autopsy showed reticulo-endothelial proliferation, this led to a diagnosis of aleukemic reticulo-endotheliosis

In the early lesions there was a loss of the epidermis near the follicle with lymphocytic infiltration around the follicle and the sweat glands Some large pale cells in the background were not noted at the first examination, and the disorder was regarded as pyoderma At the borders of the more advanced lesions there was perivascular infiltration with polymorphonuclear cells, small lymphocytes and some larger mononuclear cells The main portion of the lesion had a loose fibrillary structure with dilated capillaries and some nonspecific infiltration, the predominant cell was larger, round or oval and had a clear cytoplasm, from some of these cells narrow processes extended into the fibrillary tissue The nuclei were pale, and many were reniform or bilobed (figs 4 and 5)

Chronic aleukemic reticulo-endotheliosis with cutaneous changes has been reported by a number of observers There seems to be nothing characteristic about the macular, papular and nodular eruptions which have been described, the hemorrhagic tendency is not so evident as in the acute forms Other clinical features are also nonspecific there are usually general weakness, fever, anorexia and loss of weight The liver, spleen and lymph nodes may be enlarged In cases of this as in those of the acute condition the diagnosis is usually not made until there is opportunity to examine the tissues microscopically

Case 6 is reported as an example of chronic reticulo-endotheliosis because of the final pathologic observations The condition is representative of the large group of disorders in which the clinical, hematologic and pathologic processes at various times resemble various diseases Many observers classify such a disorder as a nonspecific lymphoblastoma

CASE 6—A 38 year old woman suffered from weakness and menorrhagia, resulting in severe anemia Examination of the blood showed that only 10 per cent of the white cells were mature, the count was 38,000 A tentative hematologic diagnosis of acute myeloblastic or stem cell leukemia was made There were petechiae on the conjunctivae and hemorrhagic areas on the uvula and buccal mucosa, retinoscopic examination showed petechiae and hemorrhagic areas An eruption on the posterior surface of the neck (fig 6) consisted of a large number of elevated disklike nodes which acquired an increasingly deep blue color On the legs and arms were tender deep-seated red nodules resembling those of erythema nodosum

Sections of the papules showed an edematous fibrillary cutis with only a few small lymphocytes and a few larger cells having small dense nuclei or two or

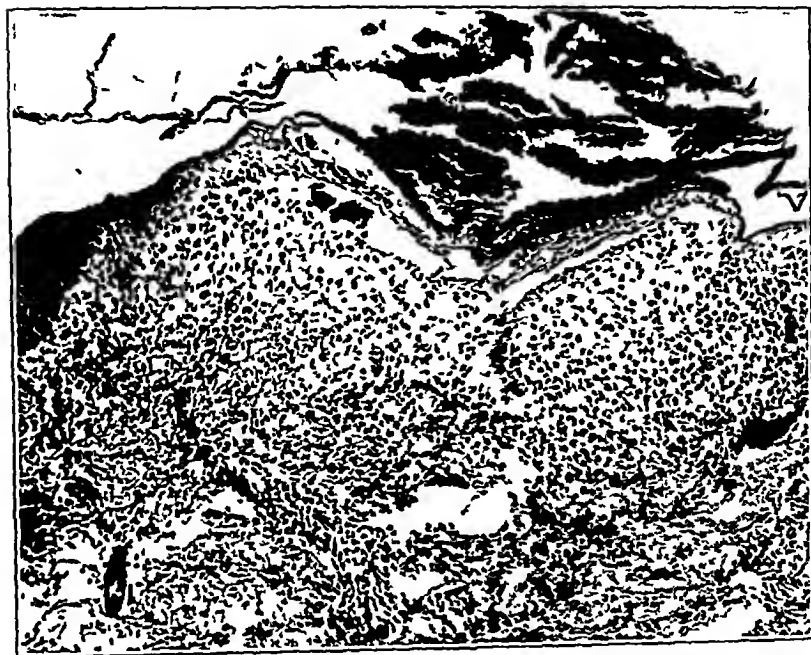


Fig 4 (case 5) —Low magnification of a section from a pustular lesion

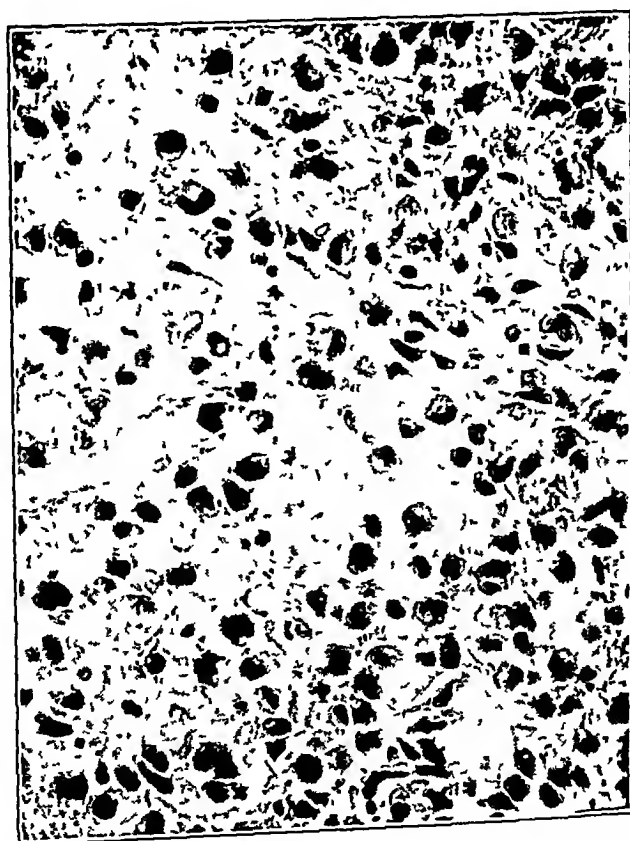


Fig 5 (case 5) —Higher magnification of a section showing a loose structure with large reticular cells and many monocytes

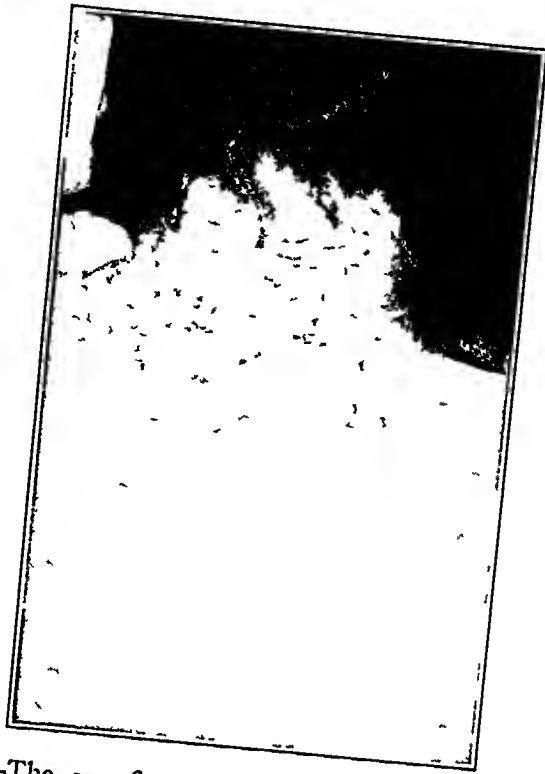


Fig 6 (case 6) —The specific indurated papular eruption on the neck was accompanied by nodules on the arms and legs

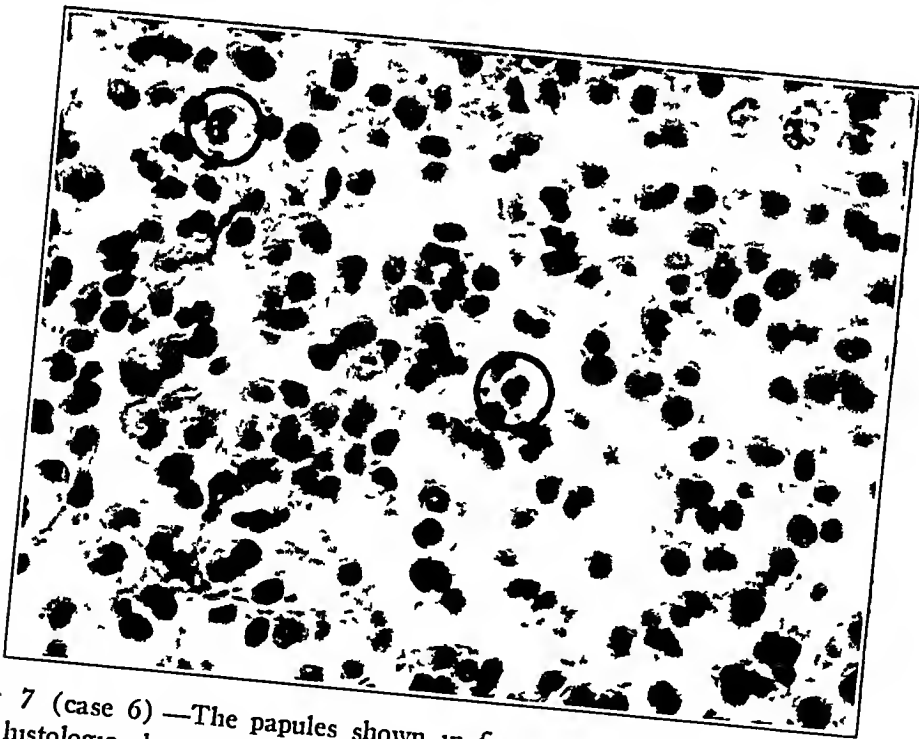


Fig 7 (case 6) —The papules shown in figure 6 exhibit a close resemblance to the histologic changes seen in monocytic leukemia cutis and in acute reticulo-endotheliosis. Note the adult monocytes as well as many immature cells and the loose reticular structure

more such nuclei. In the middle third of the cutis there were some areas of necrosis and a heavy cellular infiltrate consisting of polymorphonuclear cells and small lymphocytes, larger cells having large, pale nuclei were attached to the reticulum (fig 7)

Such papular and nodular eruptions are not infrequently observed in chronic reticulo-endotheliosis, but they do not have any specific clinical features. The earliest lesions on the neck resembled those of erythema multiforme because of the central edematous elevation and the surrounding papule.

Two other cases of reticulo-endotheliosis were observed in which the eruption was the most striking feature of the disease. The ulcerated lesions in these two cases were similar in appearance although the course was much less chronic in the first (case 7) than in the second (case 8)



Fig 8 (case 8)—Chronic ulcers of reticulo-endotheliosis

In the latter case the eruption was for many months the only demonstrable sign of disease.

CASE 7—For six months a 28 year old man had been suffering from vague symptoms, such as transitory facial paralysis, swelling of the forehead which later subsided and weakness sufficient to interfere with walking. About one month before admission to the hospital there appeared on the face, neck and scrotum inflammatory lesions which broke down and discharged pus, he also suffered from fever and loss of appetite and of weight. There were generalized lymphadenopathy and splenomegaly. The skin was icteric, and there were numerous petechiae on the trunk and extremities. There was an eruption of the neck and cheek consisting of crusted ecthymatiform lesions. On the scrotum and thighs were ten punched-out necrotic ulcers having a profuse purulent drainage, not much inflammatory reaction was visible or palpable. The course was febrile. The blood counts on admission were normal though it was noted that the lymphocytes resembled those seen in benign lymphadenosis. Several days later the total number of white cells was 4,000, and 65 per cent were large, atypical mononuclears.

In addition to numerous lymphocytes and red blood cells, sections of skin showed many large mononuclear cells with dark reniform and bilobed nuclei. These cells were superimposed on a loose reticular structure.

CASE 8—An 18 year old boy presented an eruption which began as a blister on the right calf and then darkened and enlarged to a lesion 3 cm in diameter (fig 8). During the following week the lesion dried and central sloughing occurred. A number of similar lesions appeared, and all stages of the eruption were visible on the left foot, face, neck and hands. The ulcerated lesions were sharply margined and had a firm base with central necrosis, each lesion had a red areola. General examination demonstrated nothing of significance except a palpable spleen and enlarged axillary lymph nodes. The white blood cell count was 8,000, and the differential count showed 60 per cent lymphocytes. A culture of the blood was sterile. After a few days in the hospital the patient remained free from new lesions for two months, then lesions again appeared on the legs, the eruption being accompanied by a high fever. Repeated examination failed to establish a diagnosis. Cultures of the blood were repeatedly sterile.

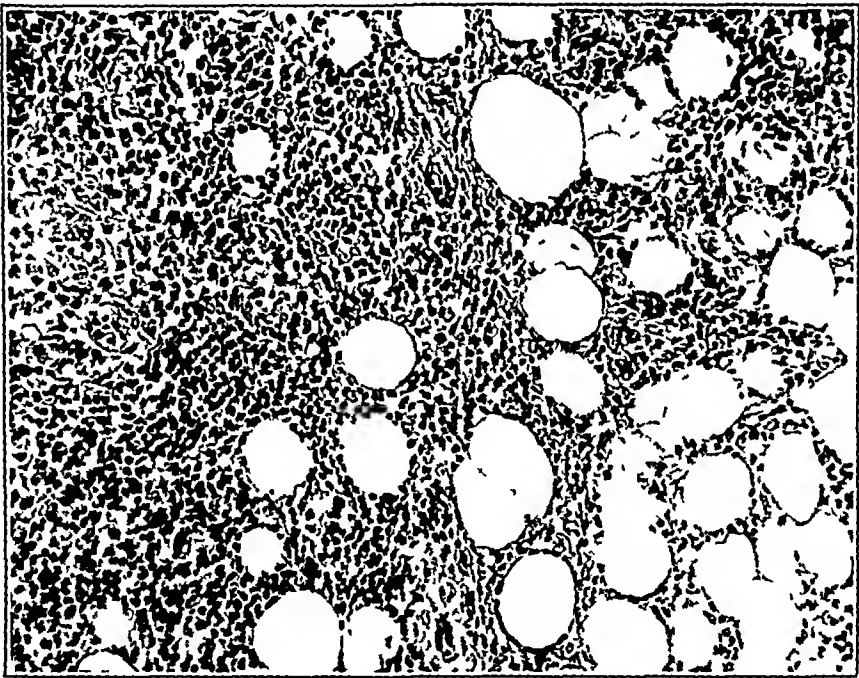


Fig 9 (case 8) —Section from an ulcer of chronic reticulo-endotheliosis showing the resemblance to erythema induratum. Giant cells were present. The infiltrate consists of lymphocytes and granulocytes. The large clear cells in the upper right corner are reticular cells.

The fever was of a remittent character like that seen in cases of lymphogranulomatosis or typhoid. The Widal reaction was negative on several occasions. One month before he died the patient began to bleed from the nose and mouth, and at times he was irrational. He had several attacks of abdominal pain associated with distention. The white blood cell count ranged from 3,000 to 8,000, and the percentage of lymphocytes alternated between 30 and 60, there was no sign of immaturity of any of the white cells.

The cutaneous eruption became rather quiescent during the last weeks of life except that two lesions on the leg persisted as deep necrotic ulcers with overhanging borders, the largest was 7 cm in diameter. A study of the lymph nodes at autopsy showed a diffuse reticular hyperplasia with some rounding out of the

reticulum cells suggesting that they might be taking part in blood formation. The bone marrow also showed numerous reticular cells. The final diagnosis was aleukemic reticulo-endotheliosis.

Tissue examined early in the course of the disease showed necrosis extending nearly to the subcutis. There was perivascular lymphocytic and polymorphonuclear infiltration at the borders, and the infiltrate was replacing the adipose tissue below. Nests of larger cells with clear, oval nuclei were at first regarded as epithelioid cells. There were also areas of hemorrhage (fig 9).

Later in the course of the disease a new lesion showed almost complete replacement of the cutis by a loose reticulated granulation tissue with giant cells and an occasional large fat cell. There were areas of hemorrhage and some nests of lymphocytic infiltrate. Polymorphonuclear cells were also present. Within the loose connective tissue framework were many larger cells, some round



Fig 10 (case 8)—Section removed later in the course of the disease, showing more specific changes with monocytoïd infiltration.

and some irregular with projecting fibrillary processes. The multinucleated giant cells were fixed to the reticular framework by fibrillary processes. In a few areas the granulation tissue was more cellular and resembled a rather loose fibroblastic proliferation (fig 10).

In the last two cases the disorder represents a necrotic ulcerative tendency which seems to have a few definite characteristics. There may be a history of preceding lesions, as in the case in which hemorrhagic bullae were observed (case 8) or the ulceration may be the first change noted. These ulcers are tender but not extremely painful. The base is flat and necrotic, the borders sharp and the edges undermined. The purulent discharge subsides in a few days, but the lesions persist.

unchanged for many weeks. There is little surrounding inflammation. In the earlier months of the disease the lesions may heal with scarring. Later lesions persist and show no evidence of any tendency toward granulation or epithelization. In early stages the microscopic changes are inflammatory and associated with perivascular cellular infiltration, the presence of giant cells and necrosis. Later the tissue seems to lose its original power to react, and only a loose fibrillary granulation tissue is observed.

DIFFERENTIAL DIAGNOSIS

The diagnosis of monocytic leukemia presents no great difficulties. The angina, febrile course and hemorrhagic tendency make one immediately suspicious of acute leukemia, and the hematologic examination should establish the diagnosis. The cutaneous lesions are usually non-specific, consisting of petechiae and areas of hemorrhage, although specific exanthems also occur. These macular and papular exanthems must be differentiated clinically from the syphilitic roseola and the macular exanthematous eruptions associated with acute and chronic infectious diseases. In the chronic forms of monocytic leukemia the subcutaneous nodules and the hemorrhagic tendency immediately suggest the necessity for study of the blood.

In cases of the strictly aleukemic forms of reticulo-endotheliosis antemortem diagnosis has seldom been possible, but a competent hematologist can recognize the liberation of reticulo-endothelial cells into the blood stream in some cases when the normal white blood cell count has not been exceeded. The necrotic ulceration observed in cases 7 and 8 seems to provide the most distinctive cutaneous feature in the chronic aleukemic phase. Microscopic examination of a cutaneous lesion may rule out other diagnostic possibilities, but the polymorphous cellular infiltrate, loose reticular structure and proliferation of the large cells of the reticulum have not previously been regarded as diagnostic.

Generalized papulonecrotic hemorrhagic eruptions provide the most striking clinical feature of acute aleukemic reticulo-endotheliosis. Such eruptions are not diagnostic, and one must consider a pyoderma associated with septicemia. In some instances, as in case 9, the diagnosis may not be clear until the internal organs have been examined.

CASE 9—A generalized eruption of six weeks' duration was observed in a child 5 months of age. The eruption consisted of small punched-out necrotic ulcers, from 0.5 to 1.0 cm in diameter, some of which were hemorrhagic and some gangrenous. There were a number of infiltrated erythematous nodules on the forehead and eyelids. A few necrotic ulcers were seen on the palate. The white blood cell count was 1,700 and 2,500, respectively, on two examinations. Staphylococci were present in the blood and spinal fluid and in material from a furuncle; the internal organs showed evidence of staphylococcal septicemia.

In the upper portion of the cutis were many dilated vessels and a swollen cellular connective tissue. There was cellular infiltration with small and large mononuclear cells. Between the cutis and the subcutis were necrotic areas surrounded by an unusual granulation tissue having a loose edematous framework with polymorphic and lymphocytic infiltration as well as many larger cells with clear light-staining cytoplasm and round or oval nuclei.

This child presented necrotic lesions of the oral mucosa and a generalized eruption consisting of discrete papular and pustular lesions, many of which were hemorrhagic. The decreased white blood cell count was considered an aleukemic manifestation. A final diagnosis of staphylococcal septicemia was made after bacteriologic studies and sections of tissues had ruled out leukemia and reticulo-endotheliosis.

In case 10 there was a similar clinical picture consisting of a generalized pustular eruption, hemorrhagic tendency, septic course and a terminal decrease in the white blood cell count. There might have been considerable difficulty in classifying this eruption if the diagnosis of chronic myelogenous leukemia had not previously been established beyond doubt.

CASE 10—A boy aged 9 years had received treatment for chronic myelogenous leukemia for fifteen months when there developed an extensive furunculosis associated with an abscess of the axilla and septicemia. Culture of the blood and local lesions showed staphylococci. Hemorrhage into the furuncles resulted in heavy black crusting, there was also bleeding from the mouth and nose. The white blood cell count, which had been as high as 340,000, dropped to 300 during the last few days of life, and in the last twenty-four hours of the patient's life no white cells were seen in smears of the blood.

In the upper portion of the cutis there was considerable lymphocytic infiltration, and many red blood cells were seen, the elastic tissue was not disturbed. In the lower portion of the cutis and in the subcutis were many necrotic areas surrounded by loose edematous connective tissue the cells of which contained large, pale nuclei. There was some replacement of the adipose tissue by lymphocytic infiltrate. The microscopic picture was not that usually seen in furunculosis, nor was it identical with the specific cutaneous changes described in cases of myelogenous leukemia.

An additional instance in which knowledge of the early course was of help was one of generalized herpes zoster (case 11) occurring in a patient with chronic lymphatic leukemia. If the patient had not been seen until after the eruption had become generalized it would have been difficult to differentiate this eruption from the conditions previously described.

CASE 11—A 48 year old man who had been treated for chronic lymphatic leukemia for three years had received high voltage roentgen therapy on numerous occasions. Solution of potassium arsenite U S P was also administered. Six weeks later there developed typical herpes zoster of the lower left portion of the thoracic region which developed into a generalized vesicular eruption (fig 11).

and progressed to ulceration and hemorrhage. There were numerous lesions on the visible mucous membranes. There was a definite increase in the proportion of immature white blood cells during the rapidly fatal course of the disease.

Gross and microscopic examination of the nervous system showed no hemorrhage into the root of the thoracic nerve corresponding to the area of zoster, although there was some lymphocytic infiltration in the meninges and diffuse glial proliferation was observed. Sections of the skin did not differ from those in other cases of severe herpes zoster except by the presence of a few immature cells in the infiltrate at the base of the vesicles.

Spiegler¹⁰ in 1908 described a case of lymphatic leukemia in the course of which generalized herpes zoster developed. A total of nineteen cases of such a condition have now been recorded, in only one of which it was associated with myelogenous leukemia. Somewhat similar disorders have been described by Barney,¹¹ Brunauer,¹² and Phila-



Fig 11 (case 11)—Generalized herpes zoster in a patient with lymphatic leukemia. The vesicular lesions became hemorrhagic and necrotic, and the outcome was fatal.

delphy and Haslhofer.¹³ The eruptions have tended to be more severe than the usual generalized herpes zoster, being hemorrhagic or gangrenous in most of the cases and resulting fatally in nearly half of them. In cases in which death did not occur the eruption was frequently associated with an exacerbation of the leukemia.

Several attempts have been made to determine the cause of zoster eruptions in leukemia. Hemorrhage into the ganglion or lymphocytic

10 Spiegler. *Wien klin Wchnschr* 21 156, 1908.

11 Barney, R. E. *Leukemia Cutis Resembling Herpes Zoster*, *Arch Dermat & Syph* 25 1150, 1932.

12 Brunauer. *Case Presentation*, *Zentralbl f Haut- u Geschlechtskr* 46. 413, 1933.

13 Philadelphia, A., and Haslhofer, L. *Varicellen bei leukamischer Lymphadenose*, *Arch f Dermat u Syph* 169 502, 1934.

infiltration of the meninges or even of the nerve tissue has been observed. No changes which might be regarded as specific leukemic manifestations were found in the nervous system in case 11.

Damm¹⁴ in 1931 and Katz¹⁵ in 1932 reviewed the literature on zoster associated with leukemia, a total of twenty-seven cases are included in their reviews. Other cases have been reported by Craver and Haagensen,¹⁶ Arzt,¹⁷ Brandt¹⁸ (two cases), Marcus¹⁹ (two cases) and Pionpe,²⁰ Zeisler²¹ in 1928 mentioned having observed one case. In none of these cases was there any difficulty in recognizing the condition, but there is considerable similarity between the clinical appearance of these disorders and the generalized papulonecrotic eruptions associated with reticulo-endotheliosis. Case 11 of this series is reported not only because it is interesting in this respect but also because the disorder was an unusual leukemia which has not received the attention in the American literature which it appears to deserve. Montgomery²² discussed it together with the nonspecific eruptions of the lymphoblastomas and was the first to mention it as a common observation.

PATHOLOGIC PROCESS

The pathologic changes observed in the specific cutaneous lesions of monocytic leukemia are rather characteristic. The epidermis is normal or nearly so, in the earlier lesions cellular infiltration is seen chiefly in the perivascular areas and surrounding the appendages. The character of this infiltration is the diagnostic feature, the reaction consisting chiefly of mature and immature monocytes (fig 1). There are large cells having an abundant cytoplasm. The immature forms have dark nuclei, which may be reniform or bilobed, in the more mature cells there are large notched or oval nuclei and the cytoplasm is frequently

14 Damm, P. Om den aetiologiske sammenhæng mellem zoster generalisatus leucaemi og varicellen, Ugesk f læger 93 1279, 1931

15 Katz, F. Zoster bei Leukämie, Arch f Dermat u Syph 164 561, 1932

16 Craver, L. F., and Haagensen, C. D. A Note on the Occurrence of Herpes Zoster in Hodgkin's Disease, Lymphosarcoma and the Leukemias, Am J Cancer 16 502, 1932

17 Arzt. Herpes Zoster gangrenosus et generalisatus bei mit Arsen behandelte leukämischer Lymphomatose, Zentralbl f Haut- u Geschlechtskr 44 505, 1933

18 Brandt. Herpes Zoster generalisatus, Acta dermat-venereol 14 514, 1933

19 Marcus, K. Två fall av zoster generalisatus, ett vid lymfatisk leukemi och ett vid aleukemisk lymfadenose, Finska lak-sällsk handl 75 429, 1933

20 Proppe, A. Sammelreferate über Zoster, Dermat Ztschr 69 39, 1934

21 Zeisler, in discussion on Ormsby. Herpes Zoster Associated with a Generalized Varicella-Like Eruption, Arch Dermat & Syph 17 140 (Jan) 1928

22 Montgomery, H., in Christian, H. A., and Mackenzie, James. Oxford Medicine, New York, Oxford University Press, 1936, vol 14, chap 1-A, p 336

granular Although the recognition of monocytes is essential for the diagnosis, even an inexperienced observer can recognize the polymorphous cellular infiltrate as being different from other pathologic processes. The notching of the nuclei and the large size of the cells distinguish the condition from lymphatic leukemia. The difficulty in differentiating monocytic leukemia from myelogenous leukemia is apparent from a study of the cases described in this paper, accurate cytologic knowledge is necessary, or one may depend on the hematologic diagnosis from smears of the blood (fig 12). The absence of Dorothy Reed cells and eosinophils differentiates this disease from Hodgkin's lymphogranulomatosis.



Fig 12—In myelogenous leukemia cutis the general structure resembles that of monocytic leukemia and reticulo-endotheliosis. The immature cells are difficult to differentiate, and large reticular cells are present in both conditions. The presence of immature and mature eosinophilic granulocytes as pointed out in a case of myelogenous leukemia seems to be the most obvious differential point.

Loveman⁵ has pointed out that the cellular infiltrate extends between the connective tissue fibers and does not replace them as in the more solid areas of infiltration seen in other types of leukemia (fig 2). He mentioned the irregular shape of the cells and the tendency to produce pseudopods, features which were particularly well demonstrated in the cases of chronic reticulo-endotheliosis described in this paper. He also emphasized the lack of practical value in application of the oxidase reaction to tissues removed from patients with monocytic leukemia.

There is fairly general agreement among the various observers as to the pathology of the cutaneous lesions of reticulo-endotheliosis. The

changes in the epidermis are secondary to disturbed nutrition. There is reticular proliferation in the cutis and infiltration with large mononuclear cells, observations which conform with the descriptions of the pathologic changes observed throughout the reticulo-endothelial system in cases of such disorders.

In sections from the skin of the patients whose cases are reported in this paper the early cutaneous changes appeared around the vessels and appendages of the skin and consisted of infiltration with small lymphocytes and polymorphonuclear leukocytes. At this stage the observations are not specific, although Bingel²³ mentioned that the general structure is looser than in lymphoma, this being apparently an early sign of the change in character of the connective tissue.

Later the involvement was most intense in the lower portion of the cutis and extended even into the subcutaneous tissue. The supportive tissues no longer resembled collagenous connective tissue, the fibrillary structure was replaced by a reticular network resembling embryonic mesenchymal tissue. Between the fibrils there were large round, oval or polygonal mononuclear cells some of which had long processes extending into the reticular network. The cytoplasm and nuclear structure stained lightly, and the nucleus was large and round or oval. In addition to these cells which seemed closely related to the reticular framework, there were round cells having a darkly staining small eccentric nucleus, such cells have also been described by Erber²⁴. Many large clear cells having a moderately dense reniform or bilobed nucleus were observed, these cells resembled intermediate forms in the monocytic series (figs 5 and 7).

Stains for elastin are of little help in the study of these diseases because they show only the absence of elastin fibers in the infiltrated and granulomatous areas and degeneration of these fibers in the corium at the border of the pathologic process.

In some instances of reticulo-endotheliosis large giant cells are observed, but they seem to be of no great aid diagnostically.

The pathologic changes observed in the skin of patients with reticulo-endotheliosis are easily distinguished from those of lymphatic leukemia.

The changes observed in the skin of patients with monocytic leukemia are similar to those of acute and chronic reticulo-endotheliosis. In certain phases of the lesions it seems impossible to differentiate these two diseases. In both there is a loose framework of reticular cells and fibrils, and the free cells are chiefly those of the monocytic series.

23 Bingel. Monozytenleukämie? *Deutsche med. Wchnschr.* 42 1503, 1916

24 Erber, L. J. Ueber sogenannte Retikuloze mit Fettspeicherung, *Virchows Arch. f. path. Anat.* 282 621, 1931

In patients with myelogenous leukemia and also in infants suffering from acute sepsis similar processes may be observed. Under these conditions the connective tissues of the skin apparently return to their embryonal functional state and produce a reticular framework and immature free cells. The resemblance to reticulo-endotheliosis is even closer when a septic condition is superimposed on myelogenous leukemia (fig 11). In none of these conditions is the proportion of monocytes in the infiltrate so high as in monocytic leukemia or reticulo-endotheliosis. In all of them the structure is less reticular and more cellular and mature fibroblasts are more numerous. The reason for the similarity of these pathologic changes is the close genetic relationship between reticulum cells, monocytes, histiocytes and fibroblasts.

The reticular proliferation and intermediate cell forms observed in the skin of patients with monocytic leukemia and reticulo-endotheliosis may be regarded as further support for the view that the specific cutaneous lesions of leukemia develop *in situ* and are not the result of metastases or infiltration from the blood stream.

HISTIOCYTOMA

Histiocytoma is described as a localized form of cutaneous reticulo-endotheliosis, the etiology and significance of this condition are not known. The histiocyte is regarded as a fixed connective tissue cell closely related to the monocyte of the blood because of their common origin from the reticulo-endothelial cell. The proliferating cells of histiocytoma are more highly differentiated than those observed in the cutaneous lesions associated with leukemic or aleukemic reticulo-endotheliosis, and the structure of the former is much more compact.

SUMMARY

No one theory of the differentiation of white blood cells is acceptable to all hematologists or pathologists. Downey's theory of such processes is particularly helpful in explaining the relationship between the monocytes and other cells of the blood and between monocytic leukemia and reticulo-endotheliosis. This theory is reviewed briefly, and the cases herein reported are discussed under his classification.

The clinical and microscopic observations in eight cases of monocytic leukemia and reticulo-endotheliosis associated with cutaneous changes are described.

The difficulties in the clinical diagnosis of generalized hemorrhagic papulonecrotic eruptions are emphasized by a comparison of such an eruption occurring as a manifestation of acute aleukemic reticulo-endotheliosis with furunculosis associated with myelogenous leukemia, with staphylococcic septicemia, and with a similar eruption which rep-

resented generalized herpes zoster in a patient with chronic lymphatic leukemia. Because of the interest in cases of zoster and leukemia reported in the foreign literature, the available information on this subject is summarized.

A type of chronic cutaneous ulceration observed in two cases of chronic reticulo-endotheliosis may be one of the characteristic lesions of this disease.

The essential feature of monocytic leukemia cutis is the infiltration with mature and immature monocytes. Such cells may be recognized by their large size and notched nuclei occurring together with other distinctive features. Acute or chronic reticulo-endotheliosis is characterized by the loose structure of the lesion, there are large reticular cells having vesicular nuclei, and within the reticular framework are large free mononuclear cells. A polymorphic infiltrate may be present.

The resemblance between the pathologic changes in the specific cutaneous lesions of monocytic leukemia and of reticulo-endotheliosis is regarded as further support for the view that reticulo-endotheliosis is an aleukemic manifestation of monocytic leukemia.

THE SUDORIPAROUS GLANDS

I THE ECCRINE GLANDS

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Success in therapy for diseases of the skin demands a more intimate knowledge of the histology, physiology and function of the healthy skin. With this in view, the need for a careful study of the various dermal systems becomes apparent.

Mumford¹ emphasized the fact that constant changes are taking place in the superficial vascular system in response to various stimuli, and he expressed the belief that similar alterations are undoubtedly occurring in the activity of the sudoriparous glands, the output of which is subject to wide variations not only in different persons examined under similar circumstances but also in the same person examined at different times. These variations apparently depend on certain inherent physical and mental characteristics and on the metabolic requirements of the moment, resulting from altered internal or external physical influences or from both.

Steno² in 1683 seems to have been the first to mention the cutaneous openings of the sudoriparous glands, a year later Grew³ also called attention to them. However, it was not until 1834 that the adult sweat glands were described by Breschet⁴ and by Roussel de Vauzème. Gurlt⁵ in 1835 and Robin⁶ in 1845 published valuable contributions on the subject.

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1 Mumford, P. B. Simple Form of Sudorimeter, *Brit J Dermat* **39** 256 (June) 1927

2 Steno, quoted by Poirier, Paul, and Charpy, A. *Traité d'anatomie humaine*, ed 3, Paris, Masson & Cie, 1912, vol 5, pt 2

3 Grew, quoted by Poirier, Paul, and Charpy, A. *Traité d'anatomie humaine*, ed 3, Paris, Masson & Cie, 1912, vol 5, pt 2

4 Breschet, J., and Roussel de Vauzème. *Recherches anatomiques et physiologiques sur les appareils tégumentaires des animaux*, *Ann d sc nat*, September 1834, pp 167 and 321

5 Gurlt. *Vergleichende Untersuchungen über die Haut des Menschen und der Haus-Säugethiere, besonders in Beziehung auf die Absonderungsorgane des Haut-Talgcs und des Schweisses*, *Arch f Anat, Physiol u wissensch Med*, 1835, p 399

(Footnotes continued on next page)

EMBRYOLOGY

The sudoriparous glands have a histogenesis similar to that of the sebaceous glands, thus two essentially different types are formed

In the hairless regions the sudoriparous glands arise directly from the cutaneous ectoderm, while in the hairy regions the gland originates from the hair anlage. In the evolution of the rudiment of the sudoriparous gland in the hairless regions, three stages are recognized

Stage of the Sudoriparous Rudiment—In an embryo of the fourth month one notices first on the hands and feet full straight buds on the

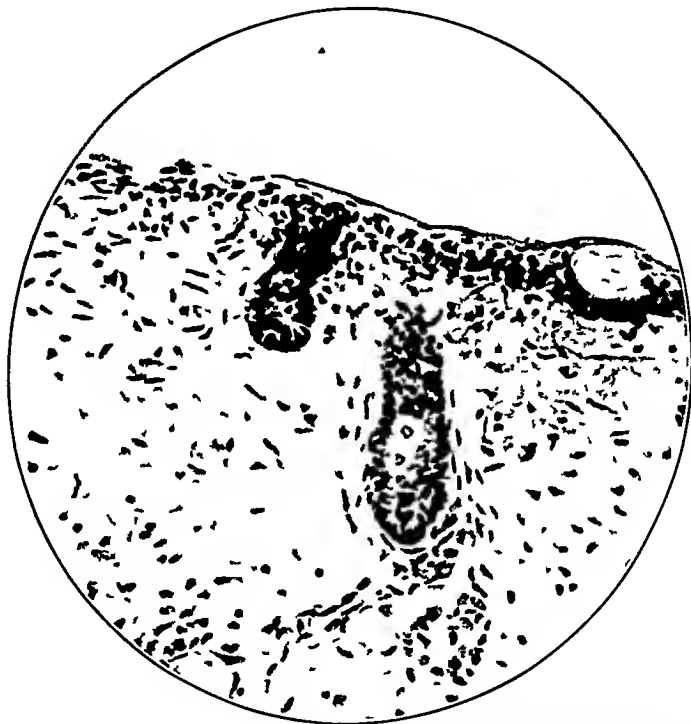


Fig 1—A section from a $5\frac{1}{2}$ month fetus, showing the ectodermal origin of a sudoriparous gland. To the right may be seen an early stage in sebaceous gland development. Hematoxylin and eosin, $\times 300$

top of the primary crests of the ectoderm, which are derived from the basilar layer. These buds are yellowish and grow perpendicularly into the dermis.

The absence of connective tissue around the epithelial bud suffices to differentiate the hair germ from the sudoriparous germ. The hair germ is further differentiated by its white color and its obliquity to the tegumentary surface.

6 Robin. Note sur une espèce particulière des glandes de la peau de l'homme, Ann d sc nat, 1845

The sudoriparous germinal layer appears first in the hairless regions and later in the hairy parts. Development occurs earlier on the palmar surfaces of the fingers than on the dorsal surfaces, this is especially true of the third finger.

During the fifth month the deeper extremity of the sudoriparous anlage becomes somewhat thicker, bending on itself to form a hook, the concavity of which is directed toward the surface of the skin. This hook twists on itself more and more.

Differentiation of the Excretory and the Secretory Segment—The formation of the glomerulus begins at this stage. The secretory seg-



Fig 2—A section from a 6½ month fetus, showing a later stage in the development of a sudoriparous gland. The coil has partly formed. Note the sebaceous gland above. Hematoxylin and eosin, $\times 200$.

ment, slightly thickened and solid at first, becomes hollowed out, forming a wide lumen which is limited by two rows of cells, one internal and one external. The first is made up of prismatically shaped glandular elements, while the second is made up of very thin cells, which later become myo-epithelial cells.

The lumen of the excretory duct appears during the sixth or seventh month, or after the formation of the lumen of the glomerulus. Some time elapses before the development of the vascular network which surrounds the gland.

Formation of the Excretory Orifice—During this stage the gland becomes longer, and the glomerulus rolls up more and more. Up to this point the excretory segment, though hollowed out, does not open on the surface of the skin, nor is there any evidence at this time of a depression at its external termination. It is only in the seventh month (fetal) that there is a complete passage way through the epidermis. This passage way is in the form of a spiral, the turns of which become more and more numerous and the caliber of which becomes lessened. Sweat can appear on the surface of the skin as soon as the emissary orifices become opened. Because of the lateness of the time at which this occurs, one cannot believe that the sweat glands play a rôle in the formation of the amniotic fluid.

Sweat glands occurring in those regions covered with hair usually arise from the hair anlage. These glands appear at the same time as the hair germ and lengthen in the form of a cord much thinner than that of the hair. This cord appears above the rudiment of the sebaceous gland, later becoming hollowed out, and occasionally it pours out its secretion within the hair follicle. Usually, however, the gland gradually becomes separated from the hair follicle, its orifice moving away to open directly on the surface of the skin.

ANATOMIC, RACIAL AND OTHER CONSIDERATIONS

Morphology—The sudoriparous glands are made up of a long tube, the deep end of which terminates in a cul-de-sac and the superficial extremity of which opens on the surface of the skin to form a pore.

The sudoriparous tube is made up of two parts: first, an excretory part, or glomerulus, which is rolled on itself like a ball, and second, a tubule made up of two segments and having the function of carrying to the outside products elaborated by the glomerulus. The deep segment pierces the corium in a straight or slightly curved line and is called the sudoriparous passage.

Location—The sweat glands occur all over the surface of the skin, except on the anterior surface of the nails, the labia minora, the inferior parts of the labia majora, the internal surface of the prepuce, the glans and the internal part of the pinna of the ear. Some add to this list the skin of the eyebrow and parts of the integument where the muscles of the skin take their insertion, such as the region of the forehead, the cheek and the alae of the nose.

Everywhere else the sudoriparous glands are found at the surface of the skin, even on the caruncula lacrimalis and on the external surface of the pinna of the ear, where their presence was formerly denied.

Although the number of the sweat glands opening at the surface of the skin has been carefully estimated, there exists a wide variation in the count (from 2,000,000 to 15,000,000).

Their distribution is most uneven. They are rare on the external surface of the pinna of the ear and on the eyelids and are more numerous on the anterior than on the posterior surface of the body and the flexor than on the extensor surfaces of the limbs.

Sappey⁷ counted 120 glands per square centimeter where the epidermis was thin, but this number increased to 371 where the epidermis was thick, such as the palms and soles. In the axilla they are supposed to be even more numerous.

Krause⁸ counted the number of glands per square inch in various parts of the skin and found the following values: the soles, 2,700 per square inch (62 sq cm), the palms, 2,700 per square inch, the dorsum of the hand, 1,500 per square inch, the thorax, abdomen and arms, 1,100 per square inch, the dorsum of the foot, 900 per square inch, the cheeks and thighs, from 500 to 600 per square inch, the posterior surface of the neck, back and buttocks, from 400 to 600 per square inch.

Position and Size—The glomerulus of the sweat gland can easily be recognized by its yellowish or pinkish color which makes it stand out from the white surrounding tissue. Its level in the skin is subject to considerable variation. Occasionally the glomeruli, alone or in groups of from four to six, occupy the entire thickness of the corium as on the nucha of the neck and the upper part of the back. In this location they are called intradermal. More frequently the glomeruli occur beneath the dermis within the panniculus adiposus, as on the extremities, hands, feet, areola of the mammary gland and genitals and in the axilla. In the palm the level of the glomeruli varies, and here they may be either intradermal or hypodermal.

The size of the sweat glands varies. They have been classed as large, medium and small, according to the volume of the glomerulus.

The larger glands are those occurring in the axilla and on the forehead. Their diameter varies from 1 to 4 mm or more. The most voluminous glands are those on the nipple which hypertrophy during pregnancy. Medium-sized glands have a diameter from 300 to 500 microns and are found in the axilla and on the anterolateral parts of the body. Small glands are no larger than from 100 to 200 microns and are found on most of the parts of the body, either isolated or mixed with the large and medium-sized glands.

Racial factors are said to influence the size and number of the glands. In the Negro, whose skin resists high temperature, they are especially well developed, while the reverse is said to be true in the Fuegians.

⁷ Sappey, M. P. C. *Traité d'anatomie descriptive*, ed. 3, Paris, A. Delahaye, 1877, vol. 3, p. 594.

⁸ Krause, W. *Allgemeine und mikroskopische Anatomie*, in *Handbuch der menschlichen Anatomie*, Hanover, Hahn, 1876, vol. 1.

Daubler⁹ stated that the size of the sweat glands of the native of tropical Africa is much greater than that of the European. Anatomic differences, such as scanty body hair, highly developed and superficial blood vessels, everted lips and large nostrils, aid in combating the high temperatures of the tropics.

Aron¹⁰ found that the sweating apparatus of the aborigines of the Philippines, the Negritos, is superior to that of the white race. This superiority is shown by the difference in the manner of sweating rather than in the amount of the sweat produced. The Negrito secretes small beads of sweat over the entire body, which soon form a thin film. As the whole surface of the body is covered by this watery film, the maximum cooling effect is obtained from evaporation.

In the case of the white man, on the other hand, sweating is practically limited to certain areas of the surface of the body. In these areas sweating may be quite profuse, but as most of the sweat drops off, comparatively little cooling results from the evaporation.

The most extreme individual variation is met in those cases in which the sweat glands are entirely lacking. Taendler¹¹ observed a man, aged 47, who had never perspired and whose body temperature rose as high as 40.8 C (105.4 F) when exposed to the sun's rays. In this case the whole ectoderm had suffered an arrest in development. The skin was smooth and thin and the teeth were limited to two incisors and two molars in the upper jaw, while the hair was extremely sparse. All the cutaneous glands seemed to be lacking, and even the hairs failed to have their accessory sebaceous glands. Injections of pilocarpine failed to cause any production of sweat.

HISTOLOGY OF THE ECCRINE GLANDS

The difference in the morphology of the glomerulus and the sudoriparous duct readily becomes apparent when one studies the histologic features of the two parts.

Glomerulus—Under low power magnification, the glomerulus when sectioned appears to be formed of a number of cavities, placed side by side. These cavities, having a rounded or elliptic shape, are in reality only the cross-sections of the various segments of the glomerular tube.

Under a higher magnification one sees that the glomerulus is surrounded by a vitreous membrane, giving rise to two layers of cells, an internal and an external.

The basal layer of the sudoriparous glands is thicker (from 2 to 4 mm) than the stratum lucidum of the epidermis, with which it is

9 Daubler, K. Die Grundzuge der Tropenhygiene, Berlin, O. Enslin, 1900, cited by Aron¹⁰

10 Aron, Hans. Philadelphia J. Sc. 6 101, 1911

11 Taend'er. Munchen med. Wchnschr. 1900, p. 1587

continuous. It gives the same reactions as the latter, such as a blue color with hematoxylin. Its external surface is in relation with the connective tissue cells and the elastic fibers of the dermis. Its internal surface may occasionally have fine crests which interlock with those of the peripheral pole of the glomerular cells.

The external layer of the glomerular epithelium is made up of muscular cells of epithelial origin, that is, myo-epithelial cells. This is an unusual example of muscular tissue arising from the ectoderm. Placed between the basal layer and the internal cells of the glomerulus, these myo-epithelial cells appear fusiform, being directed obliquely to the axis of the tube, around which they describe an elongated spiral. Because of their obliquity, these muscular fibers act as longitudinal as well as circular fibers, thus having the power to shorten the secretory tube and at the same time to reduce its transverse diameter.

These myo-epithelial cells are composed of a cell body and a nucleus. The latter is elongated in the long axis of the cell, and, projecting on the internal surface of the cell, it comes in contact with the glandular cells. The cell body is composed of two parts: (1) a clear internal part surrounding the nucleus, called perinuclear protoplasm, and (2) an external fibrillary part, situated at one side and coming in contact with the basal layer. It represents a truly contractile element, its surface has long crests which encroach on the vitreous membrane and remain firmly attached to it.

Histologists are not in accord regarding the relationship between the myo-epithelial cells. According to Renaut,¹² they are placed as a continuous sheet and completely separate the glandular epithelium from the basal layer.

The glandular or internal layer of the glomerulus is made up of a single row of prismatic cells, placed perpendicular to the vitreous membrane. The base of these glandular cells is directed toward the periphery of the glomerular tube, where it comes in contact with the basal membrane when the myo-epithelial cells are absent at that point. When the muscular cell is developed, the glandular cells are either at a distance from the vitreous membrane or are attached to the vitreous by flat prolongations which wind in between the muscular cells so that they are surrounded by glandular elements on three sides. The apical pole of the sudoriparous cell is turned toward the lumen of the glomerulus, and its lateral surfaces are in contact with the lateral surfaces of the neighboring cells.

Fañanás¹³ has shown by Golgi's method that the glandular lumen is prolonged between the two faces of adjoining epithelial cells, as inter-

12 Renaut, J. Dispositif anatomique et mécanisme de l'excrétion des glandes sudoripares, *Ann de dermat et syph* 5 1101, 1894.

13 Fañanás, S. Terminación de los tubos secretonos de las glándulas sudoríparas, *Riv trimest microg* 1:42, 1896.

cellular canaliculi, radial in direction, which can be followed to the neighborhood of the basal layer. The intercellular canaliculi, according to Poirier and Charpy,¹⁴ are permanent structures surrounded by covering fillets. The intracellular canaliculi, however, are transitory structures excavated in the cytoplasm of the secreting cells.

The glandular cells have a rounded nucleus, with a nucleolus about half-way up the cell. A pair of micronuclei is located in the cytoplasm near the nucleus. The cellular body is bare, granules of various sizes are scattered in it, which are of two types, some being made up of fat while others, after being acted on by xylene and turpentine, are colored black with hematoxylin or osmic acid and are perhaps pigment granules.

Granules of unequal size, which stain red with carbolfuchsin, have been noted in the sudoriparous cells. As these granules reduce osmic acid after having been acted on by fat solvents, they cannot be regarded as fat granules, nor are they believed to be related to pigment.

However, a part of the cutaneous pigments reduces osmic acid as does fat. If treated first with chromic acid, this pigment, in contrast to fat, no longer reduces osmic acid.

Junction of the Glomerulus and Excretory Segment—At the point where the excretory tube is a continuation of the glomerulus, the vitreous layer occurs without interruption. The myo-epithelial cells, which later disappear in the sudoriparous canal, are still present in this transitional zone and may have a bifurcated end. The epithelium proper presents here an unusual appearance with its two layers of cells. The cells of the deeper layer are polygonal or hemispheric and noticeable because of their large size and clearness. The cells of the superficial layer forming the edge of the lumen are small and deeply colored and usually have a thin extension which is insinuated between the deeply located cells and occasionally is prolonged to the myo-epithelial cells. The superficial part which surrounds the lumen appears as a refractile membrane.

Between the glomerulus and the excretory canal there is a zone of transition which is characterized by the fact that the glandular cells which are in one layer of the glomerulus have a tendency to become superimposed. Some of the cells become voluminous and keep their initial position, while others take on the shape of a nail, as though compressed by the deep cells. At the foot they are separated and intercalated between the deeper cells. Thus they are in contact with one another because of their flared-out head and constitute a continuous layer.

¹⁴ Poirier, Paul, and Charpy, A. *Traité d'anatomie humaine*, ed 3, Paris, Masson & Cie, 1912, vol 5, pt 2.

The Sudoriparous Canal—A slight thickening of the glomerular tube sometimes marks the beginning of the sudoriparous canal, which is formed of a double row of epithelial cells implanted on the basal layer. This basal layer of the canal touches on its external surface the connective tissue of the dermis and the elastic network which surround the sudoriparous gland. Two layers of epithelial cells are placed on the basal layer, the external one being continuous with the basal layer of the epidermis and the internal one lining the lumen of the canal.

The cells of the external layer are elongated and have a clear protoplasm similar to the cells of the external sheath of the hairs.

The cells of the internal layer are thicker, their free pole is surrounded by a narrow band and covered by a rigid membrane which is deeply stained by osmic acid. One concludes that there is no secretory phenomenon in the sudoriparous canal. Near the interpapillary epithelial bud the epithelium of the sudoriparous canal may be stratified and have from three to four layers. The canal itself is generally round or oval throughout its entire length.

The sudoriparous canal loses its wall as it enters the epidermis and is known as the sudoriparous passage. A simple opening, bordered on all sides by epidermal cells, makes up this sudoriparous passage.

In the malpighian layer this passage is either straight or rolled in the form of a spiral and limited by cells arranged in two or three concentric layers around the passage. These cells are flat and filled with granules of eleidin. The internal layer of these cells has a cuticle.

In the stratum corneum the sudoriparous passage forms a spiral with its turns close together and ends in a so-called sweat pore, which is placed obliquely to the surface of the skin.

In the dermis the course of the duct is more or less straight and almost vertical, that is, perpendicular to the surface of the skin. When the epidermis is thin, the duct runs through an interpapillary bud, traverses the malpighian layer in a straight line and spirals only within the stratum corneum to end in a pore.

When the epidermis is thick, as on the palms and soles, the dermis is furrowed with dermal crests the summit of which has two papillae. The sweat duct enters the epidermis at the summit of the epidermal bud, separating the two papillae. It twists on itself while penetrating the malpighian layer and describes from twenty to thirty circles of a spiral in the epidermis. These circles are constant and especially close together in the stratum corneum but are not exactly superimposed one on the other.

The cutaneous orifice of the excretory duct opens at the top of the papillary crests by a pore which has a double obliquity, that is, oblique to the surface of the skin and to the axis of the canal. Therefore, foreign bodies do not readily enter it.

Histophysiology of the Sweat Secretion—Glandular and muscular cells form the essential parts of the glomerulus. These two types of cells may be activated separately through the influence of different agents, and it is possible to study the cellular modifications which accompany the secretory acts and the muscular contractions of the glomerulus. Heynold¹⁵ has been given credit for the discovery that the glomerulus is responsible for the formation of sweat.

Secretory State A gland which has just secreted an abundant amount of sweat has small and low glandular cells. The protoplasm is clear and shows no striations. The nucleus is large and forms the greater part of the cell. The lumen of the glomerulus is wide and filled with an irregularly shaped coagulum which is made up of slightly modified plasma. This plasma is of an albuminous nature and occasionally contains cellular débris. The periglandular connective tissue contains scattered red and white cells which may pass into the products of secretion.

Exhausted State If the sudoriparous glands are examined while fixed in the contracted state, certain definite changes are noticed in the secretory part of the gland. This segment has a narrow, irregular lumen which is slightly smaller than normal. Certain modifications in the form of the glandular cells have taken place with reference to their structure and relation to each other. They are deformed and frequently flattened and contain large vacuoles. The cells on opposite sides of the gland come in contact with one another, so that the lumen of the glomerulus seems partitioned off by epithelial bridges. The myo-epithelial cells are in contact with each other, and because of their contraction a shortening of the glomerular tube occurs, which causes a narrowing of the lumen.

Periglandular Connective Tissue—The connective tissue surrounding the gland is rich in elastic fibers. In the secretory segment one sees a few elastic fibers penetrating into the glomerulus, which are called intraglomerular fibers, but most of the fibers are placed around and perpendicular to the glomerulus so that a series of anastomosing rings are formed. These rings are attached to each other by longitudinal fibers, which limit their separation. In the dermal portion of the excretory canal the elastic fibers change their direction, so that they gradually blend with the elastic network of the papillary body.

Blood Vessels—Many vascular twigs go to each glomerulus to form a network on its surface, the polygonal meshes of which measure from 20 to 40 microns. This network, because of its very richness, is distinguished from the vessels of the surrounding connective tissue.

Fine twigs from the periglandular network penetrate to the interior of the glomerulus, but they do not enclose the sudoriparous tube tightly in their meshes. All the glomerular vessels are embedded within con-

15 Heynold Arch f path Anat u Physiol 61 72, 1874

nective tissue-forming arches, which are joined together by curved anastomoses.

The vessels of the excretory canal have two origins. Those destined to the deep part of the excretory canal come from the glomerular network, but those which supply the superficial part of the excretory canal come from the subpapillary plexus.

Lymphatics—The lymphatics coming from the sudoriparous apparatus join the vessels from the subpapillary network.

Nerves—Definite experimental proof of the existence of sweat nerves was first obtained by Goltz¹⁶ in experiments on stimulation of the sciatic nerve in cats.

Early observers, including Herrmann,¹⁷ Ficatier¹⁸ and others, have shown that a rich nerve plexus exists around the gland which is made up of fibers without myelin, the fibers traverse the membrana propria and end in the musculature. The nerve fibrils have enlarged end-pieces, which come in contact with the excretory epithelium and are placed between the glomerulus and the excretory canal within the transitional epithelium.

Ranvier,¹⁹ in speaking of the periglandular plexus, stated that this network is very fine and that its tight meshes are long and perpendicular to the long axis of the secretory tube. Some of the fibrils go forth from it to end in the myo-epithelial layer. Sfameni²⁰ in a later article stated that there is a nerve network in the membrana propria of the glomerulus which gives off fibers ending on the secretory epithelium. He expressed the belief that the nonmyelin network described by other writers is vasomotor in function.

Histologically and anatomically, the arrangement of the sweat fibers resembles that of the vasoconstrictor fibers, and, reasoning from analogy, one might suppose that a general sweat center exists, but positive evidence of such a center is lacking.

Howell,²¹ in speaking of sweat centers in the central nervous system, stated that the fact that secretion of sweat may be brought about by stimulation of the afferent nerves or by direct action on the central nervous system, as in the case of dyspnea, implies the existence of

16 Goltz, Arch f d ges Physiol 11 71, 1875

17 Herrmann, G. Particularités relatives à la structure des glandes sudoripares, Compt rend Soc de biol 17-365, 1879

18 Ficatier, J. F. A. Etude anatomique des glandes sudoripares, Thèse de Paris, no 113, 1881

19 Ranvier, L. Le mécanisme des sécrétions, J de microg 10 544, 1886

20 Sfameni, P. Des terminaisons nerveuses dans les glomérules des glandes sudorifères de l'homme, Arch ital de biol 29 373, 1898

21 Howell, W. H. Textbook of Physiology, ed 6, Philadelphia, W. B. Saunders Company, 1915, p 861

physiologic centers controlling the secretory fibers The precise location of the sweat center or centers has not, however, been satisfactorily determined

The action of the nerve fibers on the sweat glands cannot be explained as an indirect effect, for instance, as a result of a variation in the flow of blood In human beings it is known that profuse sweating may often accompany a pallid skin, as in terror or nausea, while, on the other hand, the flushed skin associated with fever is characterized by the absence of perspiration

There seems no doubt that the sweat nerves are genuine secretory fibers causing a secretion in consequence of a direct action on the cells of the sweat glands

The sweat glands may be made to secrete in many ways other than by direct artificial excitation of the sweat fibers, for example, by extreme heat, dyspnea, muscular exercise and strong emotions and by the action of such drugs as pilocarpine, muscarine, strychnine, nicotine and physostigmine In all such cases the effect is supposed to result from an action on the sweat fibers, either directly on their terminations or indirectly on their cells of origin in the central nervous system If the nerves going to a limb are cut, exposure of that limb to a high temperature does not cause secretion, showing that the change in temperature alone is not sufficient to excite the gland or its terminal nerve fibers

One must suppose, therefore, that high temperature acts on the sensory cutaneous nerves, possibly the heat fibers, and reflexly stimulates the sweat glands Although external temperature does not directly excite the glands, it should be stated that it affects their irritability by direct action either on the gland cells or on their terminal nerve fibers

Experimentation leads us to assume that there are spinal sweat centers, but whether these are few or represent simply the various nuclei of origin of the fibers to different regions is not definitely known It seems reasonable to conclude that in addition to these spinal centers there is a general regulating center in the medulla

HERPES ZOSTER GENERALISATUS

REPORT OF TWO CASES OCCURRING IN PATIENTS WITH LYMPHATIC LEUKEMIA AFTER TREATMENT WITH ROENTGEN RAYS

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BROOKLYN

Herpes zoster associated with a generalized eruption simulating varicella has been until recently a rather uncommon occurrence. In the greater number of cases reported the disorder has appeared in a patient with a disease belonging to the group of lymphoblastoma (Hodgkin's disease, lymphatic leukemia, myeloid leukemia, lymphogranuloma, etc.)

REPORT OF CASES

CASE 1—M H, a man aged 40, a furrier, born in Russia, came to the dispensary of the Jewish Hospital on April 19, 1933, complaining of swellings around the neck and in the armpits of three weeks' duration.

Family History—The family history was irrelevant except for the fact that one brother had died of tuberculosis of the lungs at the age of 35.

Examination—The glands of the neck were enlarged and swollen, the reaction extending to the angles of the jaw. Substernal dulness was noted. The spleen was enlarged from 2 to 3 fingerbreadths below the costal margin. The axillary and inguinal glands were also enlarged.

Examination of the blood gave the following results. The bleeding time was two minutes, the coagulation time, three minutes, the tourniquet test was positive. The hemoglobin content was 85 per cent. There were 70,000 platelets, 6,000,000 red cells and 36,000 white cells. The differential count showed 15 per cent polymorphonuclears, 0.8 per cent polymorphonuclear eosinophils, 1 per cent monocytes and 83 per cent small and large lymphocytes. The uric acid content of the blood was 3.5 Gm per hundred cubic centimeters.

The basal metabolic rate (Sanborn) was + 57 per cent. The patient's height was 164 cm, his weight was 87.5 Kg, and the surface area was 1.95 square meters. The duration of the test was fifteen minutes. The pulse rate was 76, and the respiratory rate, 17.

Roentgen examination of the chest showed considerable broadening of the superior mediastinal shadow, which had a nodular appearance. There was also

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a separate opaque mass extending from the root to the base of the right lung and adjacent to the cardiac border. No apparent involvement of the lungs was discernible.

Subsequent studies of the blood gave the following results

	May 22, 1933	July 15, 1933	Sept 1, 1933	March 23, 1934	Sept 4, 1934
Hemoglobin	62 per cent	80 per cent	70 per cent		59 per cent
Color index					0.8
Red cells	5,200,000		4,600,000		3,500,000
Platelets	70,000		100,000		
White cells	10,000	34,000	41,600	60,000	10,500
Polymorphonuclears		15 per cent	17 per cent	15 per cent	12 per cent
Small and large lymphocytes		85 per cent	83 per cent	85 per cent	88 per cent

Treatment and Course—From June 28, 1933, to March 22, 1934, the patient received high voltage roentgen therapy to the enlarged glands and to the spleen. At that time examination showed enormous enlargement of all the lymph nodes—postauricular, cervical, mediastinal, axillary, inguinal and retroperitoneal. The spleen was enlarged, measuring 6 fingerbreadths.

The patient was seen again on April 2, 1934, at which time he presented an extensive eruption (see figure) beginning at the fifth lumbar and first sacral vertebrae on the left side and extending over the left hip and buttocks to the midline of the lower portion of the abdomen and the groin. The eruption consisted of groups of vesicles from 0.5 to 1 cm. in diameter, some of which had ruptured and many of which were gangrenous. The lesions were surrounded by a ring of erythema. Distributed over the entire body and over the face, trunk and limbs were numerous discrete vesicles, pustules and papules which simulated varicella. The mucous membranes were free from lesions.

The lesions of zoster cleared up, leaving pitted scars and pigmentations. The patient could not remember whether or not he had had varicella in childhood.

CASE 2—B. R., a woman aged 53, a housewife, was admitted to the Jewish Hospital on July 9, 1934, complaining of pain in the legs, generalized pain and weakness and difficulty in walking in a straight line.

Examination—Examination showed enlargement of the inguinal and axillary glands on both sides. The liver and spleen were enlarged also. The Romberg sign was positive. When the patient walked she fell to the left.

The blood count showed 3,790,000 red cells, 64 per cent hemoglobin and 156,800 white cells. The differential count showed 1 per cent polymorphonuclears and 98 per cent small lymphocytes.

Repeated blood counts showed no change in the lymphatic condition.

Roentgen examination showed some turgescence of the anterior thoracic wall. Roentgen examination of the chest, however, showed no evidence of mediastinal tumor.

Neurologic study revealed a possibility of an intracranial lesion involving either the vestibular pathways or the cerebellum.

Treatment and Course—The patient received high voltage roentgen therapy to the neck, axillae, inguinal regions, spleen and pituitary region for one year.

She returned to the hospital on July 20, 1935, after a rest of two weeks, complaining of burning pain and itching behind her right ear. She stated that she first noticed pimples on that area about one week previously.

Examination showed grouped vesicles, some of which were hemorrhagic and crusted, in the right postauricular region and extending on the posterior aspect



Varicelliform lesions distributed over the entire back. Gangrenous herpes zoster affecting the region of the fifth lumbar vertebra.

of the ear. Distributed over the left eyebrow, upper and lower lips, chin, chest, abdomen and back were numerous discrete papules and pustular lesions, some of which were surrounded by erythema. No lesions were found on the buccal mucous membranes.

COMMENT

According to Schoenfeld,¹ the first case of herpes zoster with aberrant vesicles was described by Lipp in 1889 at the congress of the German dermatologic society in Gratz, Austria. He described lesions of zoster affecting the trunk, arms and legs which appeared after a severe attack of zoster pectoralis.

Haslund² reported the case of a patient who presented herpes zoster affecting the left dorso-abdominal region and had vesicles on the trunk and extremities. This patient also had lesions on the tongue and mucous membranes.

Parounagian and Goodman³ reviewed the literature to 1923 and reported only one case of herpes zoster with disseminated lesions occurring in a patient with lymphatic leukemia.

Fischl's⁴ patient was examined post mortem, at which time there were found a generalized adenopathy and leukemic infiltration of the internal organs. The gasserian ganglions were found to be infiltrated with leukemic cells.

Jadassohn⁵ presented a patient with herpes zoster and a varicelliform exanthem who had lymphatic leukemia. An attack of zoster gangraenosus in the region of the first and second branch of the trigeminal nerve was associated with a moderate varicelliform exanthema disseminated over the entire trunk. The patient stated that he had not had varicella. Jadassohn was of the opinion that the attack of herpes zoster had no connection with the lymphatic leukemia.

Jadassohn's patient was presented again three months later.⁶ The leukemia had improved after roentgen therapy, but the patient had edematous swelling and redness on the face in the scars of the herpes zoster and more or less sharply limited, flat and elevated, irregularly round, bluish red and slightly transparent infiltrations. Surrounding the infiltrations were several lentil-sized red papules. Similar papules were disseminated on the trunk in the exact spots where vesicles had formerly been present. The lesions subsided somewhat after roentgen therapy, but they continued to be noticeable. Jadassohn could not decide whether the tumefactions were due to the blood residue or to the overgrowth of fixed elements in the skin.

1 Schoenfeld, in Jadassohn, Joseph. *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1928, vol 7, p 11.

2 Haslund, A. Om zona, i anledning af et tilfælde med generaliseret eruption, *Nord med Ark* 8 1, 1897.

3 Parounagian, M B, and Goodman, H. Herpes Zoster Generalisatus, *Arch Dermat & Syph* 7 439 (April) 1923.

4 Fischl. Herpes zoster generalisatus, *Wien klin Wchnschr* 24 14, 1911.

5 Jadassohn, Joseph. *Zentralbl f Haut- u Geschlechtskr* 20 23, 1926.

6 Jadassohn, Joseph. *Zentralbl f Haut- u Geschlechtskr* 20 741, 1926.

Schreus⁷ reported a case of herpes zoster occurring in a boy 11 years old after roentgen therapy had been administered for Hodgkin's granuloma. He believed his case to be the first instance of that condition reported.

Andrews⁸ presented a man aged 29, who had been treated for Hodgkin's disease with roentgen rays and arsenic and had suffered from severe zoster of the left supra-orbital region.

Ginsburg⁹ reported the case of a woman, aged 34, who after having received radium and roentgen treatment for Hodgkin's disease from July 1921 to January 1922 began to exhibit signs of spinal irritation. These signs became progressively worse until April 1923, when there developed a complete spastic paraplegia with sphincteral involvement. In July 1923 a profuse herpetic eruption developed. At first it appeared on the right side of the thorax at the level of the third and fifth dorsal segments of the spinal cord, and later it spread over the entire body, giving the appearance of typical chickenpox.

Pancoast and Pendergrass¹⁰ described four cases of Hodgkin's disease in which herpes zoster occurred during the course of the malady. All the patients had received cross-fire roentgen radiation over the involved areas. The attacks of herpes zoster occurred from four months to five years after therapy had been instituted. In none of the cases were there any varicelliform lesions. Pancoast and Pendergrass stated that the occurrence of herpetic eruption in patients with Hodgkin's disease was rare, but that such an eruption did occur more frequently than was generally recognized or taught.

Craver and Haagensen¹¹ recorded seven cases of herpes zoster observed among three hundred and twenty-nine cases of lymphosarcoma, Hodgkin's disease and leukemia and gave the figures as in the following tabulation:

Disease	Number of Cases	Number of Cases of Herpes Zoster	Percentage of Cases of Herpes Zoster
Lymphosarcoma	59	3	7.0
Hodgkin's disease	72	3	4.5
Lymphatic leukemia	108	1	0.9
Myeloid leukemia	90	0	0.0
Total	329	7	0.02

7 Schreus, H. T. *Dermat Wehnschr* 83 1606 (Oct 30) 1926

8 Andrews. *Herpes Zoster Gangrenosa in a Patient with Hodgkin's Disease*, *Arch Dermat & Syph* 15 736 (June) 1927

9 Ginsburg, S. *Hodgkin's Disease with Predominant Localization in the Nervous System (Case 7)*, *Arch Int Med* 39 571 (April) 1927

10 Pancoast, H. K., and Pendergrass, E. P. *On Occurrence of Herpes Zoster in Hodgkin's Disease*, *Am J M Sc* 168 326, 1924

11 Craver, L. F., and Haagensen, C. D. *Occurrence of Herpes Zoster in Hodgkin's Disease, Lymphosarcoma and the Leukemias*, *Am J Cancer* 16 502 (May) 1932

Craver and Haagensen did not describe a generalized varicella-like eruption in any of the cases they observed

Halle¹² observed twenty-four cases of zoster in patients with leukemia. He noted that in the majority of cases herpes zoster appeared in male patients between the ages of 50 and 70 and that often it was accompanied by herpes generalisatus. The incidence is given in the following tabulation

Type of Leukemia	Number of Cases	Male	Female	Number of Cases of Zoster Generalisatus
Lymphatic leukemia	16	13	3	11
Myeloid leukemia	5	5	0	1
Pseudoleukemia	3	2	1	0

Haack¹³ reported a case of herpes generalisatus occurring in a 67 year old woman with lymphatic leukemia. She had had symptoms of lymphatic leukemia for one year when typical herpes zoster developed along the course of the fifth nerve. There was an associated generalized varicelliform eruption. Arsenic had not been given.

The diagnosis of herpes zoster generalisatus should be a comparatively simple procedure.

The primary lesions are typical and are usually limited to certain regions of the body. The groups of zoster lesions follow the course of the sensory nerves. Often the lesions are varied in appearance, and the eruption may be accompanied by fever, adenitis, pain and tenderness. New crops may appear after the outbreak of the primary lesions. Lesions may appear on the mucous membranes, but this is an uncommon occurrence. Nobl and Steuer¹⁴ were the first to emphasize that varicelliform lesions may occur on the mucous membranes in association with an eruption of zoster. The generalized eruption simulates that observed in varicella.

PATHOGENESIS

It is generally believed that true zoster is always due to a specific virus. The disorder does not represent a trophic disturbance because the lesions develop in relation to the spinal ganglions. The eruption is probably due to the appearance of the virus at the level of the affected region. It appears that the skin is the portal of entry, whence the virus travels from the nerve endings, along the nerve sheaths, back to the spinal ganglions.

12 Halle, H. *Arch f Dermat u Syph* **159** 238, 1930

13 Haack, K. *Dermat Wchnschr* **95** 1819 (Dec 17) 1932

14 Nobl and Steuer, cited by Schoenfeld¹

According to Schoenfeld, there are three possibilities to be considered when herpes zoster is accompanied by a generalized zosteriform eruption

1 The patient has a typical eruption of herpes zoster and gets an unrelated vesicular eruption

2 The patient has a herpes zoster-like eruption which is only symptomatic of another condition already present which spreads as a vesicular eruption

3 Primary herpes zoster becomes generalized owing to lack of resistance or lack of immunity of the host

It has been shown that leukemic changes may occur in the spinal ganglion. This has been considered by many authors to be the chief rôle in the pathogenesis of zoster. Fischl⁴ described a leukemic infiltration of the gasserian ganglion. Freund¹⁵ described a case of zoster associated with hemorrhage about the gasserian ganglion and with degeneration in the ganglion. Marigonda¹⁶ in examining spinal fluid observed an increase in the number of leukocytes similar to that in the blood and therefore concluded that the spinal ganglion was affected.

SUMMARY

Two cases of herpes zoster generalisatus occurring in patients with leukemia are reported.

Herpes zoster generalisatus followed high voltage roentgen therapy. One patient (case 1) had received roentgen radiation to the region of the spleen and involved lymph glands, the other (case 2) had received roentgen radiation to the cerebellar region because the possibility of leukemic infiltration causing symptoms was considered. It becomes more apparent that zoster with disseminated lesions is not infrequently observed in association with leukemia of the aged.

225 Eastern Parkway

15 Freund, H. Arch. f. Dermat. u. Syph. **154**:476, 1928

16 Marigonda, P. Gazz. d. osp. **49**:549, 1928

INFLUENCE OF SERUM ON THE FREI TEST

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AND

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As part of a study of lymphogranuloma venereum a series of experiments have been carried out to test the action of serum from patients with clinical manifestations at various stages of the disease on Frei antigen, when serum and antigen are administered intradermally to patients known to have the disease. These experiments were prompted in a measure by the report of Reiss¹ on the antigenic property of serum from patients with early stages of the disease and by the work of Gottlieb² on the neutralizing effect on Frei antigen of serum from patients with healing inguinal adenitis. While the work was in progress Haynes³ reported the effect of serum from patients with lymphogranuloma venereum on Frei antigen, his report being based on results of intradermal injections of such serum in a small number of cases. He concluded

The mixture of Frei antigen and serum from a patient with lymphogranuloma inguinale produced the same cutaneous reaction as that to Frei antigen alone.

The intradermal injection of serum from patients with lymphogranuloma inguinale into patients showing positive reaction to Frei antigen caused no reaction, with one doubtful exception.

It is well known that there is a great variation in the local and systemic response of patients to infection with lymphogranuloma venereum. While experimental work with mice and monkeys has shown that the virus is widely disseminated after inoculation and can be recovered

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The work was aided by a grant from the Yale University Research Fund.

1 Reiss, F. A New Immunologic Reaction for the Diagnosis of Lymphogranuloma Inguinale, *Arch Dermat & Syph* **31** 215 (Feb) 1935.

2 Gottlieb, F. Neutralisation du virus de la lymphogranulomatose inguinale (maladie de Nicolas et Favre) par le serum des malades en voie de guérison. Methode de contrôle de l'intradermo-réaction de Frei, *Compt rend Soc de biol* **111** 141, 1932.

3 Haynes, H A, Jr. Value of Intradermal Injection of Serum as a Diagnostic Test for Lymphogranuloma Inguinale, *Arch Dermat & Syph* **32** 795 (Nov) 1935.

from the spleen, liver, kidneys and blood,^{3a} there is no evidence to prove that this dissemination occurs in man, nor is there any conclusive proof that there is a natural immunity in man, partial or complete

A positive Frei reaction means only that a patient has been infected with the virus of lymphogranuloma venereum and by the infection has been rendered allergic to the intradermal injection of the inactivated virus (Frei antigen). It appears that once the allergic state of the patient has been established it remains for life, though it is subject to some variation, as evidenced by the varying response of the same person to the same antigen at different times. Therefore, a positive Frei reaction demonstrates only that infection has occurred, it tells nothing about the activity of the disease in the patient tested.

The reports of Reiss, Gottlieb and Haynes raised many questions as to what, if any, demonstrable effect serum might have on the Frei test. Is the antigenic property of serum from a patient with an early stage of the disease more pronounced when the patient has an indolent, long-standing inguinal adenitis than when he has an acute infection? At what point in the healing of an inguinal adenitis do neutralizing bodies begin to appear in the serum? Does serum from a patient in whom no lesions have been present for more than a year still tend to inhibit the Frei reaction? Can serum from patients with late stages of the disease and with rectal strictures and esthiomene influence the Frei test? It was hoped that some estimation of the activity of the infection at a certain stage might be obtained by testing the effect of serum from a patient with that stage of the disease on Frei antigen when serum and antigen were injected intradermally into a patient in whom the duration and clinical activity of the disease were known.

There was another aspect of the problem on which it was hoped that some light might be shed. Repeated intradermal injections of Frei antigen have been recommended in the treatment of inguinal adenitis. If serum from patients receiving weekly injections of Frei antigen influenced the Frei reaction in other patients, some estimation of its value as a therapeutic measure might be forthcoming.

The same serums were being used to study the protection afforded by serum from patients known to have lymphogranuloma venereum when a mixture of serum and virus was inoculated into mice and guinea-pigs. As controls these mixtures of serum and virus were heated

3a Findlay, G. M. Climatic Bubo and Lymphogranuloma Inguinale, *Lancet* 2 11, 1932, Experiments on the Transmission of the Virus of Climatic Bubo (Lymphogranuloma Inguinale) to Animals, *Tr. Roy. Soc. Trop. Med. & Hyg.* 27 35, 1933. Levaditi, C., Ravaut, P., Lepine, P., and Schoen, R. Réceptivité de la souris à l'égard du virus de la maladie de Nicolas et Favre, *Compt. rend. Soc. de biol.* 109:285, 1932. D'Aunoy, R., von Haam, E., and Lichtenstein, L. The Virus of Lymphogranuloma Inguinale, *Am. J. Path.* 11: 737, 1935.

TABLE 1—Data on Serums Used for the Tests

Patient	Race	Antigen Prepared From	Stage of Infection at the Time Blood Was Drawn or the Patient Was Used for Testing	Treatment	Date on Which Blood Was Drawn	Time After Appearance of Lesions	Experiment in Which Serum Was Used	Date on Which Serum Was Used	Number of Days Serum Stored at 4 C
Dr	?		Early	Inguinal adenitis	6/25/35	2 weeks	1B	7/16/35 marked hemolysis	21
N S	White		Early	Inguinal adenitis on right side healing, draining sinus still present 12/10/35	Intradermal injection of 0.7 cc weekly of Frei antigen from 9/17/35 to 12/10/35, two courses of blis muth subacetylate	1½ weeks	3A	9/24/35	19
						5 weeks	4	12/10/35	96
							4A	9/24/35	7
						8 weeks	4	12/10/35	84
							3B	10/ 8/35	0
						9 weeks	4	12/10/35	6
						10 weeks	4	12/10/35	36
						11 weeks	4	12/10/35	49
						14½ weeks	4	12/10/35	11
							4	12/10/35	19
M G	White	8/29/35 glands	Early	Inguinal adenitis on left side, glands excised 8/27/35, wound healed 9/16/35	Intradermal injection of 0.7 cc weekly of Frei antigen from 9/7/35 to 12/10/35	2 weeks	2, 3A	9/24/35	25
						4½ weeks	4	12/10/35	102
							2, 3A	9/24/35	7
						7½ weeks	4	12/10/35	84
							3B	16/ 8/35	0
						8½ weeks	4	12/10/35	63
						9½ weeks	4	12/10/35	76
						10½ weeks	4	12/10/35	49
						12 weeks	4	12/10/35	42
						14 weeks	4	12/10/35	33
							4	12/10/35	19
P B	White		Early	Inguinal adenitis on right side, subsided without suppuration in two weeks		1 week	4	12/10/35	35
A Z	White		Early	Inguinal adenitis on right side healing, adenitis healed 6/4/35	Intradermal injection of 0.5 cc of Frei antigen weekly from 4/13/35 to 6/4/35	6 weeks	1A	5/21/35	5
						22 weeks	1B	7/16/35	61
						25 weeks	4	12/10/35	84
							1B	10/ 8/35	1

A	White	6/30/33 pus	Quiescent	Healed bilateral inguinal adenitis	Intradermal injection of Frei antigen, three doses of 0.3 cc each, 7/13/35 and 9/6/35	1 year 4 months	8/20/35	10	8/20/35	0
I D	White		Quiescent	Healed inguinal adenitis on left side	Intradermal injection of Frei antigen, three doses of 0.3 cc each, 3/28, 4/2 and 4/7/35					
W S	Negro		Late quiescent	Rectal stricture			3/15/35	Unknown number of years	8/20/35	158
A W	Negro		Late quiescent	Rectal stricture	Intradermal injection of Frei antigen, four doses of 0.4 cc each, 3/7, 3/14, 4/25 and 5/2/35		3/15/35	6+ years	8/20/35	158
I S	Negro		Late quiescent	Rectal stricture, esthomenie			8/20/35	10+ years	8/20/35	0
II J	Negro		Late	Perforations of labia and vagina	Bismuth and potassium iodide		5/16/35	Unknown 2+ years	5/21/35 7/16/35	5 61
B S	White		Late	Rectal stricture, condylomas	Intradermal injection of 0.5 cc of Frei antigen each week, Oct 1935 to June 1935		5/16/35	Unknown 5+ years	1/21/35 7/16/35	5 61
J Du	White		Late	Scar in left inguinal region, atrophy of left testicle, draining sinus in left portion of scrotum	Bismuth subsalicylate, intradermal injection of 0.6 cc of Frei antigen each on 9/17 and 9/24/35		9/17/35 10/ 3/35	30 years	9/24/35 12/10/35 10/ 8/35 12/10/35	7 84 5 68
Normal controls Repeatedly negative reactions to Frei antigen made from human pus										
II ₁					8/20/35		8/20/35	10	8/20/35	0
II ₂					9/24/35		9/24/35	2, 3A	9/24/35	0
II ₃					12/ 1/35		12/ 1/35	4	12/10/35	9
Σ					6/15/35		6/15/35	10	8/20/35	60

at 57 C for the same time as in making Frei antigen and were injected intradermally into patients known to have lymphogranuloma venereum

MATERIALS

Antigens—Three antigens of different ages were used. The first, obtained from E F (case 2⁴), was prepared from pus aspirated on Oct 17, 1934. The material for the second antigen was obtained at the first aspiration of pus from A A (case 4⁴) and had been stored in the icebox without appreciable loss of potency since July 1, 1933. The third antigen was made from an emulsion of a gland of M G, Aug 29, 1935.

Mouse Brain Virus—Three mice of generation 11 of strain G died in convulsions twelve days after intracerebral inoculation. The brains were removed and a 10 per cent emulsion with Savita broth was prepared. This emulsion (163) was centrifugated for two minutes at low speed to remove the larger particles and the supernatant fluid was used for test purposes.

The brains of three other mice of generation 12 of strain G killed seven days after intracerebral inoculation were similarly prepared (emulsion 169).

The results of the inoculations of serum and virus into animals will be reported elsewhere.

Serums—Details regarding the type and duration of the infection of the patients from whom the serums were derived, the amount of Frei antigen given intradermally, the antisyphilitic treatment given, the date on which the blood was drawn and the number of days which elapsed before the serums were used are given in table 1. Serum not used at once was stored in stoppered test tubes without a preservative at 4 C and was always tested for sterility before being used. The normal serum was obtained from one of us (M H) on three occasions, the designations H₁, H₂ being used, and from a donor (S).

PROCEDURE

Equal parts of the antigen or of the emulsion of the virus used and of the serum to be tested were mixed, and 0.1 cc was injected intradermally into patients known to have lymphogranuloma venereum. Control injections of undiluted Frei antigen, of equal parts of antigen and saline solution and of serum alone were employed. All the mixtures of serum and antigen were tested immediately after being prepared and, in most instances, after they had been allowed to stand for varying periods at 4 or at 37 C. In the case of the mixtures of serum and virus the material remaining after the inoculation of animals was heated in sealed tubes at 57 C for two hours one day and for one hour the next day as is done in the preparation of Frei antigen. It was then kept in the icebox at 4 C for ten days before the cutaneous tests were made.

All the cutaneous reactions were read and measured twenty-four and forty-eight hours after injection. An effort was made to use in any one experiment serum from patients with early and with late stages of the disease and to make tests on both patients with early and patients with late stages of the disease. Only the forty-eight hour readings are recorded in tables 2 to 5, which summarize the results obtained.

4 Howard, M E, and Strauss, M J. Lymphogranuloma Inguinale. Report of Sixteen Cases in and Around New Haven, New England J Med 212 323, 1935.

TABLE 2—Results of Tests

[illegible]

RESULTS

In the first experiment (experiment 1A, table 2) serum from a patient with an early stage of the disease in the process of healing (A Z), which had been stored five days, and serum from two patients with late stages (B S and H J) were used, the cutaneous tests were made on the same patient with an early stage, (A Z), and on two other patients with late stages (B S and A W). The serums alone failed to produce any reaction, the response to the mixtures of serum and antigen was greater than that to an equal dilution of saline solution and antigen used as control and was in each case equal to the results obtained with undiluted Frei antigen.

The same serums, stored sixty-one days, were again used (experiment 1B, table 2) to compare the results with those produced by serum from a patient with a very early stage of the disease (Br).⁵ The mixtures of serum and antigen were freshly prepared and injected within an hour into two other patients (A A and J D),

TABLE 3—Results of Tests

Experiment	Date of Experiment	Antigen Used	Date of Preparation	Patient Tested	Undiluted Antigen	Antigen and Saline Solution	Mixtures of Antigen and Serum		
							M G 8/30	M G 9/17	Control H ₂
2A	9/24/35	A A	6/30/33	M G	++++	++	++	++	++
				N S	++++	++	+++	+++	++
				J Da	++++	+++	+++	+++	++
Incubated at 37 C for 2 Hours, Kept in Icebox at 4 C for 44 Hours									
2B	9/26/35			M G	N D	++	++	++	++
				N S	++++	++	++	++	++
				J Da	N D	++++	++	++	++

A reaction of from 2 to 3 mm in diameter is indicated by ++, one of from 4 to 5 mm in diameter, by +, one of from 6 to 7 mm in diameter, by +++, and one of 8 or more millimeters in diameter, by +++++. N D indicates that the test was not done.

both of whom had healed lesions. The undiluted antigen produced a less marked response in these patients than in the previous three, but the mixtures of serum and antigen caused a reaction alike in all respects to that produced by the mixture of saline solution and antigen (control). It was not believed that the serum from the patient with the early stage of the disease (Br) in any way enhanced the local action of the Frei antigen or that the serum itself possessed any antigenic properties. The serum was markedly hemolyzed on arrival, and an intradermal injection of it given to J D, a patient with a healed lesions, resulted in a bluish red papule 4 mm in diameter without surrounding erythema. This was fading at the end of forty-eight hours, at least four days before the reactions to the other tests made at the same time began to disappear.

The difference in the reaction produced by the mixtures of serum and antigen in experiments 1A and 1B raised the question whether the storing of serum for any length of time played any part in its action on the antigen. With this in mind experiment 1C was made. In this experiment the action of freshly drawn serum as compared to that of stored serum from normal persons as well as from patients with lymphogranuloma venereum was studied. Fresh serum was obtained from a normal person (H₂), from J D, a patient with an inguinal adenitis which had been healed for over a year, and from F S, a patient with a rectal stricture and elephantiasis of the external genitalia. Serum from a normal person (S) had been stored in the icebox for sixty-six days. Serums from A W and M S,

⁵ The serum was sent by Dr H M Robinson, of Baltimore.

TABLE 4—Results of Tests

TABLE 4—Results of Tests																	
Experiment	Date of Experiment	Antigen Used	Date of Preparation	Patient Tested	Undiluted Antigen	Antigen and Saline Solution	Mixtures of Antigen and Serum										
							Control H ₂	8/30 M G	9/17 M G	9/17 N S	9/17 J Da	Serum Alone					
JA	9/24/35	M G	8/30/35	M G N S J Da	+++ +++ +++	+++ +++ +++	Incubated at 37° C for 2 Hours, Kept in Icebox at 4° C for 44 Hours										
							+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
							+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
							+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
JB	10/8/35	M G	8/30/35	M G N S J Da	+++ +++ +++	+++ +++ +++	Incubated at 37° C for 3 Hours, Kept in Icebox at 4° C for 42 Hours										
							+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
							+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
							+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
	10/10/35	M G	8/30/35	M G N S	+++ +++	+++ ++	Incubated at 37° C for 3 Hours, Kept in Icebox at 4° C for 42 Hours										
							+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
							+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
							+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
A repetition of from 2 to 3 mm in diameter is indicated by +, one of from 4 to 5 mm in diameter, by ++, one of from 6 to 7 mm in diameter, by +++, and one of 8 or more millimeters in diameter, by ++++, and																	

both of whom had late stages of lymphogranuloma venereum with rectal strictures, had been stored one hundred and fifty-eight days. Tests were made with the freshly prepared mixtures after they had been left standing at 4 C for forty-eight hours and for eighteen days, respectively. F S was a Negress with dark, thick skin, and the tests were made and the results read with difficulty, which may account in part for the variations in the cutaneous reactions recorded. From the results obtained it did not seem that serum from patients with lymphogranuloma venereum with clinically quiescent lesions had any greater effect on antigen when injected intradermally than did normal serum, regardless of the time it had been stored or of how long the mixtures of serum and antigen had stood (fig 1). The irregularities present made it apparent that many more tests were necessary before a conclusion, if any was possible, could be reached.

TABLE 5—Results of Tests

Date	Control	Mouse Brain Antigen	Serum Used		Patients Tested					
			Case	Date Drawn	M G		N S		A W	
12/10/35	Saline solution	169			+++		+++		N D	
	Saline solution	163				+				N D
	Normal serum	169	Control	12/ 1/35	++		++++	++	N D	
			H ₂							
	Normal serum	163	Control	12/ 1/35		++		++		N D
			H ₂							
		169	N S	9/ 5/35	+++		+++		+++	
		169	N S	9/17/35	++		+++		+++	
		169	N S	10/ 8/35	+++		++		++	
		169	N S	10/15/35	+++		+++		+	
		163	N S	10/22/35		+		0		0
		163	N S	10/29/35		+		0		+
		163	N S	11/21/35		++		+		+
		169	M G	8/30/35	++		+++		+	
		169	M G	9/17/35	+++		++		+	
		169	M G	10/ 8/35	+		++		+++	
		169	M G	10/15/35	++		+++		++	
		163	M G	10/22/35		++		+		0
		163	M G	10/29/35		++		+		0
		163	M G	11/ 7/35		++		++		++
		163	M G	11/21/35		+		+		++
		169	P B	11/ 5/35	++		+++		++	
		169	A Z	9/17/35	+++		+++		++	
		169	J Da	9/17/35	+		++		++	
		163	J Da	10/ 3/35		0		+		++

A reaction of from 2 to 3 mm in diameter is indicated by +, one of from 4 to 5 mm in diameter, by ++, one of from 6 to 7 mm in diameter, by +++, and one of 8 or more millimeters in diameter, by ++++. N D indicates that the test was not done.

Experiments 2A and 2B (table 3) were made with an old but potent antigen and with serum from a control (H₂) and from a patient with an early stage of lymphogranuloma venereum obtained before the glands had been excised (M G, Aug 30) and two weeks later (Sept 17) when healing of the operative wound was progressing satisfactorily. The tests were made on two patients with an early stage of the disease (M G and N S) and on one with an infection of thirty years' duration (J Da). Serum from a normal person and the antigen produced results similar to those obtained with the antigen and serum from a patient with an early stage of the disease, and neither mixture seemed to have an action greater than that which might be attributable to dilution (see control experiments with saline solution).

In experiment 3A (table 4) the tests were repeated with a freshly prepared antigen mixed with the same serums as those used in experiment 2 as well as

with serum from another patient with an early stage of the disease (N S),⁶ from a patient with a late stage (J Da) and from a normal person (H₂). Tests were made with the freshly prepared mixtures and were repeated after the mixtures had stood for some time. It was not found that serum from the patients with early stages of the disease in any way enhanced the local action of Frei antigen or that the serum itself possessed any antigenic properties.

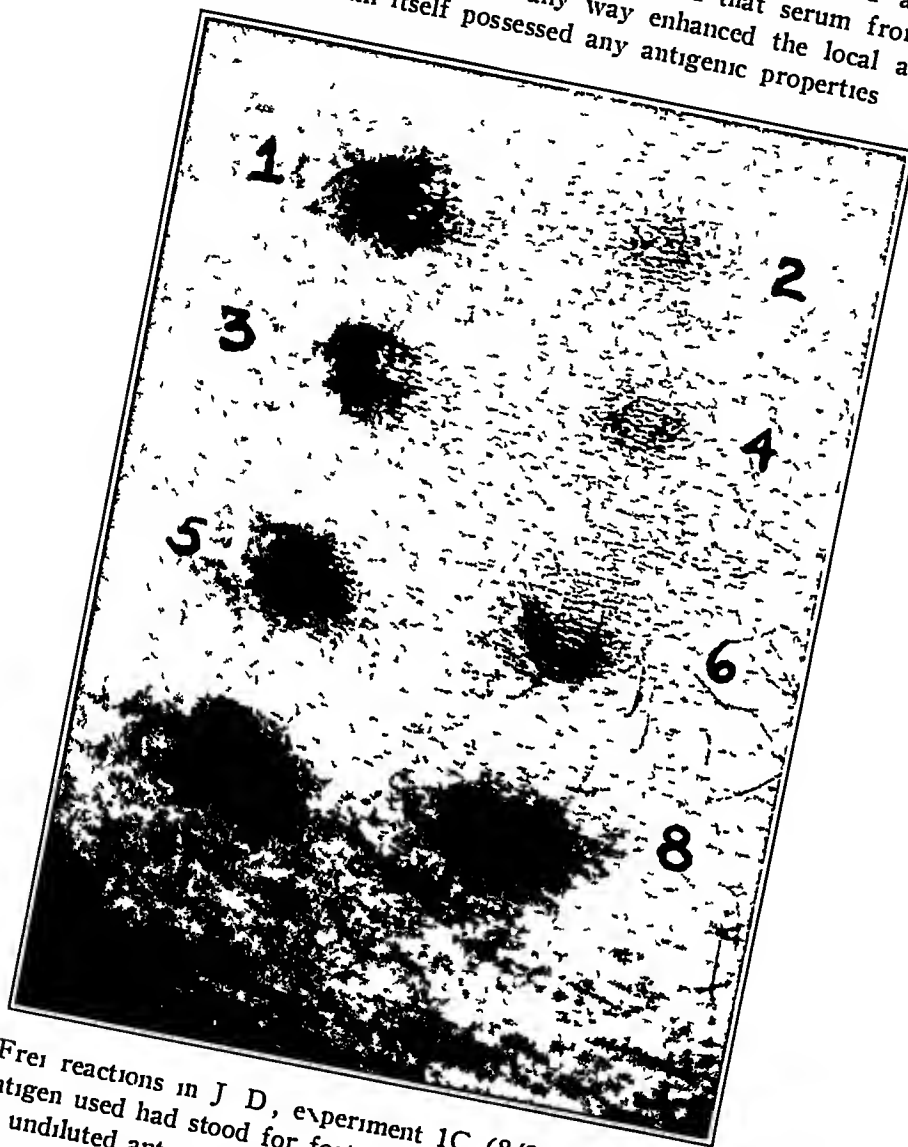


Fig 1—Frei reactions in J D, experiment 1C (8/22/1935). The mixture of serum and antigen used had stood for forty-eight hours at 4 C. The results were: 1, reaction to undiluted antigen from E F, 2, reaction to antigen and saline solution, 3, reaction to antigen and fresh serum from a normal person, 4, reaction to antigen and fresh serum from J D, 5, reaction to antigen and fresh serum from F S, 6, reaction to antigen and serum from A W stored one hundred and fifty-eight days, 7, reaction to antigen and serum from M S stored one hundred and fifty-eight days, 8, reaction to antigen and serum from a normal person (S) stored sixty-six days.

⁶ In this patient the glands were not removed surgically as in M G. The bubo had been present for about two months, and suppuration was well advanced when he was first seen. On Sept 4, 1935, 2 cc of thick greenish yellow glairy pus was aspirated. A sinus developed at the site of the puncture and continued to drain until December 1935, though the bubo became progressively smaller.

Serum obtained at later dates from the same patients with early stages of the disease (N S and M G) as healing was advancing and from a patient whose lesion had been healed for some months (A Z), as well as serum from a patient with a late stage (J Da) when used in combination with Frei antigen (experiment 3B, table 4), produced reactions as irregular as those observed previously (fig 2). No differences could be found in the effect of serum from the patients with healing lesions (M G and N S), with healed lesions (A Z) or with long standing lesions (J Da).

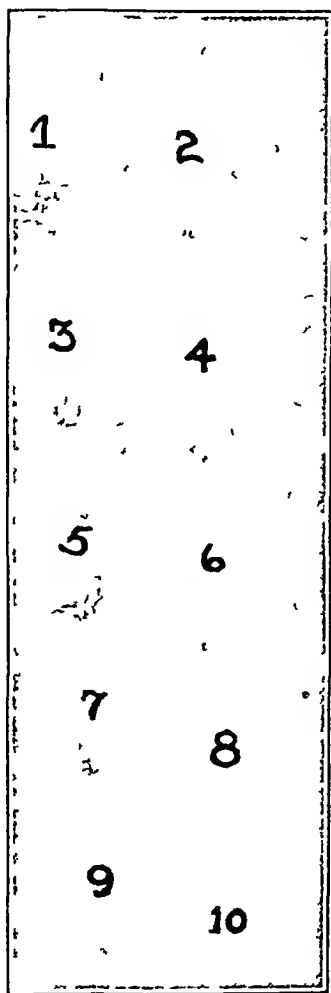


Fig 2—Frei reactions in N S, experiment 3B (10/8/1935). Mixtures of serum and antigen were injected immediately after being prepared. The results were 1, reaction to undiluted antigen from M G, 2, reaction to antigen and saline solution, 3, reaction to antigen and serum from J Da (10/3/35), 4, reaction to serum J Da (10/3/35), 5, reaction to antigen and serum from A Z (10/7/35), 6, reaction to serum from A Z (10/7/35), 7, reaction to antigen and serum from M G (10/8/35), 8, reaction to serum from M G (10/8/35), 9, reaction to antigen and serum from N S (10/8/35), 10, reaction to serum from N S (10/8/35).

Three of the patients had received intradermal injections of Frei antigen for about a month, two having received the antigen just prior to the time serum was drawn and the third having received it four months before. Two were receiv-

ing weekly intramuscular injections of bismuth subsalicylate. Therapy seemed to play no part in the results obtained.

The results of the mixtures of serum and virus made into antigens are shown in table 5. The antigenic properties of emulsion 163 (an emulsion of mouse brain) were considerably less than those of emulsion 169 but were consistently so in the control mixtures with saline solution, in the mixtures with normal serum and in those with the serums from patients with lymphogranuloma venereum tested. Serum had been collected from the two patients with early stages of the disease (N S and M G) at approximately weekly intervals for three months as healing progressed and while the patients were receiving weekly injections of Frei antigen intradermally. In N S the treatment did not seem to accelerate healing, as the sinus which formed about the site of puncture when pus had been aspirated from the gland continued to drain during this time. In M G the wound healed within two weeks after the glands had been removed, though this patient was also given continued weekly injections of Frei antigen. From the results obtained it did not seem that serum from patients with healing early lesions of lymphogranuloma venereum tended to suppress the action of Frei antigen. Nor was the difference between the reaction resulting from injection of serum from a patient with an early stage and an indolent lesion (N S) and the reaction following injection of serum from a patient with an early stage whose glands had been removed (M G) great or consistent enough to indicate that the variation was due to the clinical course of the disease. The continued use of Frei antigen in these patients did not seem to produce any effect that could be demonstrated when their serums were used in combination with Frei antigen in tests on other patients.

CONCLUSIONS

From a study of tables 2, 3, 4 and 5 it seems clear that serum from patients with lymphogranuloma venereum, regardless of the stage of the infection and of the amount or kind of treatment, had no greater effect on Frei antigen than had freshly drawn or stored normal serum. It was not found that serum from patients with early stages in any way enhanced the local action of Frei antigen nor that the serum itself possessed any antigenic properties. Serum from patients with healing lesions (A Z, N S and M G) showed no greater inhibiting effect on the antigen employed than the factor of dilution might allow (see control experiments with saline solution), nor did the continued use of Frei antigen intradermally as a therapeutic measure seem to bring about any demonstrable change in the serum. The differences obtained seemed well within the limits of variation of any group of cutaneous tests.

SUMMARY

The effect of serums from normal persons and of serums from patients with various stages of lymphogranuloma venereum who had received various treatment on Frei antigen when given intradermally was studied. The tests were made on patients known to have lymphogranuloma venereum. No inhibiting or enhancing effects were observed.

DUST FROM DICTAPHONE CYLINDERS AS A CAUSE OF DERMATITIS

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AND

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During the past fifteen months we have had under observation a patient presenting a dermatitis caused by contact with the dust from dictaphone cylinders. Since, so far as we know, no description of this type of occupational dermatitis has been given, we are presenting a short résumé of this case.



Photograph showing marked edema of the face and of the eyelids following a severe flare-up of the eruption

REPORT OF A CASE

W T, a man aged 54, consulted us on Dec 21, 1934, stating that intermittent attacks of dermatitis affecting his face, the backs of his hands and his ankles had occurred during the past eight years. The dermatitis sometimes developed suddenly and became severe enough to cause marked edema of the face and eyelids. At other times it receded and persisted for long periods as mild erythema and scaling. Periods of complete freedom had become less and less frequent in the last year or two. The clinical appearance of the eruption and the history of its behavior suggested dermatitis venenata. Questioning revealed that the disorder had first developed shortly after dictaphones were installed in the large business office in which the patient worked. Furthermore, his skin had cleared and remained well during a five month period several years before in which he had been away from the office and from dictaphones.

He was requested to bring some of the dust from his dictaphone as well as scrapings from the composition mouthpiece and from the cylinders for patch tests. He cleaned his machine and collected the materials the following day, and the next morning the dermatitis of his face flared up to the extent that his left eye was practically closed (fig)

Patch tests applied to his arm revealed positive reactions to both the dust from his machine and the scrapings from the cylinders, the reactions to the latter being the stronger. Tests with scrapings from the mouthpiece gave negative results. Subsequently scrapings from two types of cylinders used revealed a 4 plus (vesicular) reaction to the scrapings of the cylinder labeled "master wax" and a slightly less marked reaction to the other. Tests with these substances gave negative results on controls. With the cooperation of Dr. N. K. Benton, medical director of the employees' benefit fund committee of the Western Union Telegraph Company, and of the Dictaphone Corporation, aluminum stearate, stearic acid and pine tar, three of the materials used in the manufacture of the cylinders, were obtained and used for patch tests. All gave negative results, however.

The patient was otherwise in good health. There was no personal or family history of allergy. His skin was clear save for a mild chronic interdigital fungous infection of the feet. Intradermal tests with trichophyton and oidiomycin (Lederle) in a 1:100 dilution provoked no reaction. Urinalysis gave negative results.

The patient was treated with soothing topical applications and fractional doses of roentgen rays. He carefully avoided all unnecessary contact with his dictaphone, which was kept carefully cleaned for him. He improved rapidly, and by Feb. 1, 1935, was well save for a slight residual thickening and scaling of his ankles and mild pruritus of his left eyelid. He remained well until May 11, when a severe flare-up occurred on his face and forehead. This was apparently the result of his being accidentally "showered" with dust from an adjacent machine. He then remained away from work until May 20, when the attack had partially subsided. On May 21, one of us visited him at his office. During the visit the mechanism of the machine and the arrangement of the "dust pan" were demonstrated in his presence. Apparently this was sufficient to cause another, though somewhat milder, flare-up. After this he remained away from work for several days. When he returned to work he was isolated from dictaphones entirely until the latter part of July 1935. Since then he has resumed work with a dictaphone but has been in a part of the office protected from drafts and isolated as completely as possible from his machine. All the machines in the office are carefully cleaned at night and are not disturbed during the day. Under this regimen the patient has remained free from dermatitis up to the present time.

A photograph showing a severe flare-up of the eruption is given

LICHEN RUBER MONILIFORMIS (MORBUS MONILIFORMIS LICHENOIDES)

REPORT OF A CASE AND DESCRIPTION OF A HITHERTO
UNRECORDED HISTOLOGIC STRUCTURE

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AND
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The prevailing general belief that so-called lichen ruber moniliformis is a variety of lichen planus does not receive support from our investigations of a dermatosis in many respects similar to the lichen ruber moniliformis originally described by Kaposi

In the present report the name lichen ruber moniliformis is used mainly for the purpose of identification Eleven biopsy specimens from our patient failed to reveal the usual histologic evidences of lichen planus

An analysis of the cases recorded in the literature justifies the assumption that in nearly all those reported as instances of lichen ruber moniliformis the conditions were actually varieties of lichen planus However, in a small minority the disorders certainly seem to belong in another category, of the latter group Kaposi's original case and our own case appear to be outstanding instances, since the conditions in these cases were not related to lichen planus or to any other conventional dermatosis

Our interest in the case herein reported does not lie so much in the circumstance that it probably represents an instance of a hitherto undescribed dermatosis as in the fact that it confirms the contention of certain authors who asserted their belief in the nonrelationship of lichen ruber moniliformis to lichen planus

KAPOSI'S ORIGINAL CASE

Kaposi¹ in 1886 described a unique eruption in a man, aged 45, who noticed the first signs of his cutaneous disorder fifteen years previously The outstanding

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University, Dr George M MacKee, Director

Read before the Section on Dermatology and Syphilology at the Eighty-Seventh Annual Session of the American Medical Association, Kansas City, Mo., May 13, 1936

¹ Kaposi, M Lichen Ruber Moniliformis, *Vierteljahrsschrift für Dermatologie* **13** 571, 1886

feature of the dermatosis was a striking and bizarre arrangement of waxy papules, nodules and keloid-like elongated strands forming parallel ridges chiefly on the neck and flexor surfaces of the arms and legs and disposed in conspicuous vertical rows corresponding to the long axes of the neck and extremities

The similarity of the eruption to strings of pearls or of coral beads led Kaposi to apply the name lichen ruber moniliformis to this dermatosis. In addition to the elevated bandlike formations and contralateral depressions on the neck, arms and legs, there were many vertical linear lesions on the abdomen, back and buttocks and a retiform design of anastomosing, chainlike papular elements on the thighs. Other regions of the body, chiefly the chest, abdomen and back, were studded with innumerable small firm slightly elevated glistening brownish red papules, some of which had punctate central depressions. Pigmented spots having the appearance of sepia-brown puncta were profusely interspersed among the papular elements. There were no marks of scratching. Small flat papular lesions were discernible on the labial mucosa, while the buccal mucosa exhibited an adherent grayish yellow membrane. The genitalia were not affected.

In his description of the clinical manifestations Kaposi stressed the resemblance of many of the small elementary lesions to lichen planus. His study of the microscopic picture of lesions in different stages of development led him to conclude, on what is today regarded as flimsy evidence, that the histologic alterations pointed to an aberrant or anomalous variety of lichen planus. His accurate clinical and microscopic descriptions have a compelling merit, nevertheless, in the light of present knowledge a perusal of his article brings to mind the saying, "What we ardently wish, we soon believe." As a matter of fact, none of his sections exhibited the well recognized structural characteristics of lichen planus. The sections were studied by the elder Unna,² who wrote "neither the primary nor the secondary elements exhibit the structure of lichen planus. On the contrary, there is a complete disharmony between the clinical and the histologic diagnosis." Kaposi described a dense cellular infiltrate in the subpapillary portion of the corium without a trace of organization or connective tissue structure. Furthermore, fairly numerous giant cells formed a part of the infiltrate. The epidermis exhibited no pronounced evidence of hypertrophy.

Unna's dissenting opinion has been upheld by subsequent authors. As early as 1905 Radcliffe-Crocker³ said in his textbook

it is open to discussion as to whether these cases really belong to lichen planus, their general arrangement and the partial involvement of the face are against it, but Kaposi described it as a variety of lichen planus, and the others have followed him.

Kaposi's erroneous conception of the eruption he described is reflected in practically all the textbooks and in most of the contributions dealing with this and with seemingly related dermatoses.

² Unna, P. *Die Histopathologie der Hautkrankheiten*, Berlin, A. Hirschwald, 1924, p. 321.

³ Radcliffe-Crocker, H. *Diseases of the Skin*, Philadelphia, P. Blakiston's Son & Co., 1905, vol. 1, p. 429.

In summing up the situation with respect to Kaposi's original case we are forced to conclude that the dermatosis was one which simulated some of the manifestations of lichen planus clinically but reproduced none of the characteristics of that disorder that are seen microscopically. This discrepancy impressed us strongly when we discovered that in our case, too, the eruption in certain respects simulated lichen planus clinically, but no evidence of that disease was disclosed on microscopic examination.

NOMENCLATURE

In the interest of brevity and to avoid irrelevancies a review of the literature⁴ is omitted. Suffice it to say that a thorough search revealed sixteen articles and reports of cases with which the name lichen ruber moniliformis is linked.

Various designations have been utilized in connection with these moniliform dermatoses, among these are "lichen planus in anastomosing bandlets" (Dubreuilh), "lichen ruber moniliform lesions" (G. H. Fox), "lichen ruber acuminatus, verrucosus et reticularis" (Kaposi), "lichen universalis moniliformis" (von Düring), and several others.

The evidence strongly indicates that in nearly all the recorded cases the disorders were clinically aberrant or were anomalous manifestations of lichen planus, exhibiting diverse primary or elementary lesions which arranged themselves in more or less bizarre or eccentric patterns. These varieties have been familiarly designated as reticulate, anastomotic, zosteriform, striate, linear, banded and so forth. Most of them were rightly regarded as belonging to lichen planus associated with verrucous, hypertrophic, corneous, papillomatous, vegetating and other morphologically diverse elementary lesions.⁵

COMPILATION OF CASES

Of the sixteen cases reported in the literature the histologic observations are given in only seven, in these seven the microscopic examination revealed lichen planus of one or another variety with the exception of that present in Kaposi's original case. In the remaining nine cases microscopic reports are completely lacking, and the descriptions are for the most part so meager and sketchy as to permit only a nebulous visualization of the clinical features. Exceptions to the latter category are

⁴ For a review and summary up to 1923, see Sternberg, A. *Arch. f. Dermat. u. Syph.* **143** 165, 1923. A complete bibliography up to 1921 is given by Bucler, F. A. *Arch. f. Dermat. u. Syph.* **136** 117 (Sept. 12) 1921. There is an excellent discussion by Riecke, in Mraček, F. *Handbuch der Hautkrankheiten*, Vienna: Alfred Holder, 1905, vol. 2, p. 588.

⁵ In one case, Gunsett's, the retiform eruption of anastomosing bands corresponded in outline to the superficial veins of the lower portion of the abdominal wall and of the lower extremities.

the good clinical photographs of the disorder exhibited by two American patients, the case of one being reported by G H Fox⁶ in 1888 and that of the other by Hyde⁷ in 1906 and again by Hyde and Ormsby⁸ in 1910. It is strange but true that these American patients exhibited eruptions more closely resembling those of Kaposi's and of our patient than did the disorders of any of the other patients, all of whom were Europeans. In view of the unquestionable clinical similarity of the eruptions to that in our case it is unfortunate that sections were not obtained in the two aforementioned instances. For purposes of comparison the clinical-morphologic features alone lend themselves to interpretation.

REPORT OF A CASE

Mr C H, a man aged 38, a native of the United States, a florist, first consulted Dr William D Whitehead, of Scranton, Pa, in March 1935 regarding his eruption. Dr Whitehead removed several sections of the patient's skin for microscopic examination, sending the tissue to Dr J Frank Fraser, of New York, for study. (Dr Fraser did not submit a report of his histologic observations.) The patient, having changed his residence to New York, applied for treatment at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct 29, 1935.

The patient's family history was irrelevant. Physical examination revealed an appendectomy scar resulting from an operation performed in 1921. The patient was operated on for hemorrhoids in 1924 and underwent a tonsillectomy in 1926. Since that date he had been in excellent general health except for his cutaneous disease. There was no history or evidence of venereal infection.

Examination.—Examination of the heart revealed bradycardia and left axis deviation. The basal metabolic rate was 7 per cent below normal. The blood pressure was 106 systolic and 80 diastolic. The patient's height was 72 inches (182 meters), and his weight, 162 pounds (73.5 Kg). The pulse rate was 56 and the respiratory rate 16. Examination of the fundi showed that the nasal portions of the outline of the disks were blurred, otherwise the fundi were normal. The pupils were regular and reacted normally.

Roentgen examination of the skeleton revealed that the long bones were normal and the pelvis showed slight asymmetry. The sella turcica was proportionately large, being fully 20 per cent oversized in the ventrodorsal diameter, no evidence of erosions or pressure atrophy was discernible, small flecks of calcification in the pineal body were mesially placed and of no pathologic significance. Developmental variation was considered ascribable to slight glandular dysfunction, the hypophysis was relatively large. The sinuses and maxillary antrums were normal, except for slight clouding of the right maxillary antrum.

Cutaneous Condition.—The eruption was generalized, involving all regions with the exception of the anterolateral aspects of the cheeks, the nose, a portion of

6 Fox, G H. Lichen Ruber with Monileform Lesions, *J Cutan Dis* 6 312, 1888.

7 Hyde, J N. Lichen Ruber Monileformis, *J Cutan Dis* 24 85, 1906.

8 Hyde. Lichen Ruber Moniliformis, *J Cutan Dis* 28 265, 1910. Ormsby. Lichen Planus Atrophicus, *ibid* 28 467, 1910.

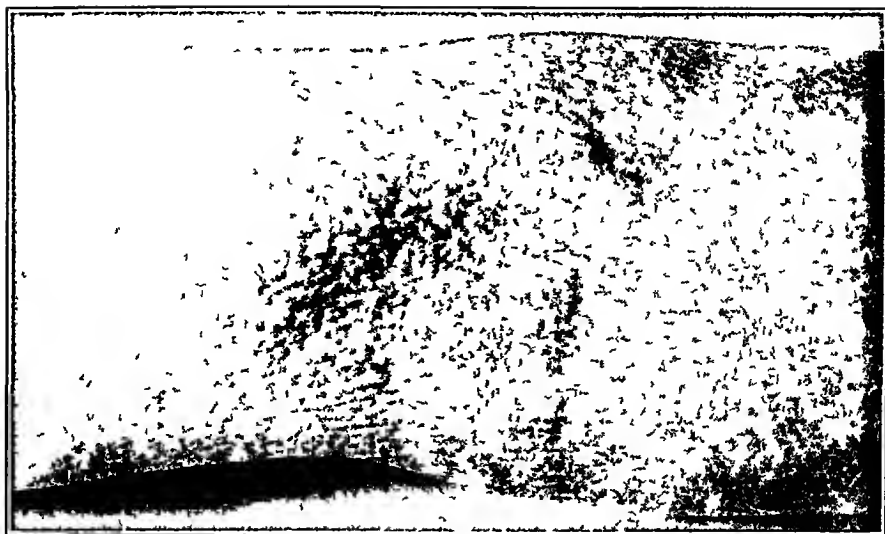


Fig 1—Lichen ruber moniliformis on the left arm



Fig 2—Lichen ruber moniliformis on the right arm

the subclavicular area and of the upper part of the sternal area of the chest, the interscapular portion of the back, the palms and soles and the glans penis. The visible mucosa and the nails were unaffected. The hair of the scalp was normal. The areas exhibiting the most conspicuous features of the eruption were the forehead, the skin below and behind the ears, the neck, the flexor aspects of the upper extremities, the backs of the hands, the axillary regions, the abdomen, the thighs, the buttocks and the lower portion of the back. The lesions were more widely scattered and less prominent on the lower extremities, from the knees to the toes. The scalp exhibited a few scattered papules. Two postoperative scars on the abdomen were entirely free from papular lesions.

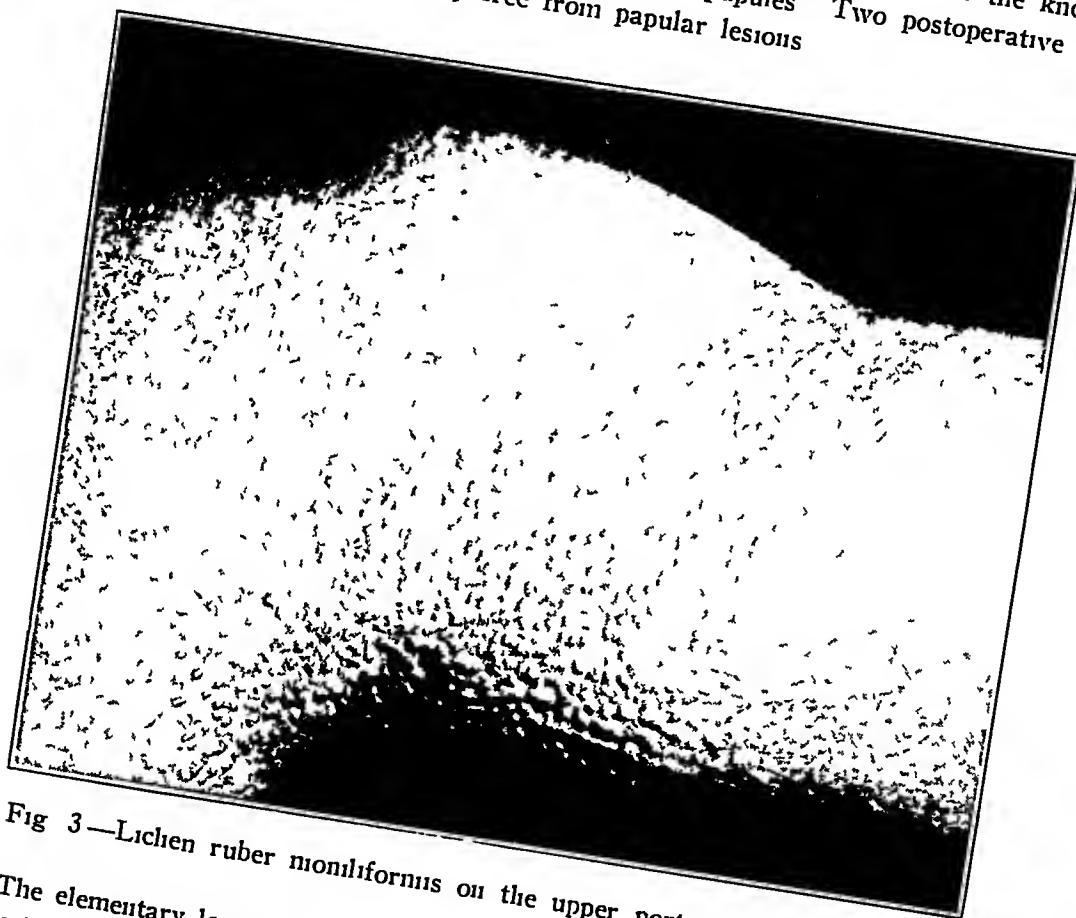


Fig 3—Lichen ruber moniliformis on the upper portion of the right arm

The elementary lesions consisted of wavy papules varying from 1 to 3 mm in diameter. Their outlines were round and dome shaped. The papules were of two types: (1) dark red and bright red elements and (2) wavy yellow milia-like elements. The red papules formed the greater part of the eruption, being present chiefly on the upper extremities, the abdomen, the back, the buttocks and the thighs. The wavy yellow papules affected chiefly the face, the periauricular areas, the middle portion of the chest and the scapular regions. All the red papules were larger, in the aggregate, than the wavy yellow papules, the latter did not exceed 2 mm in diameter. The papules were smooth and devoid of surface markings such as scales, epidermal striae or dell formations. On the face, upper portion of the back and middle portion of the chest the smaller wavy yellow elements were intermingled with the red ones. On the other areas of the body

only the red lesions were apparent except on the shaft of the penis and on the scrotum, here the papules were lighter than the normal skin on which they were situated

The consistency of all the papular elements (with the exception of those on the genitalia) was that of a keloid, the palpating finger received the impression felt

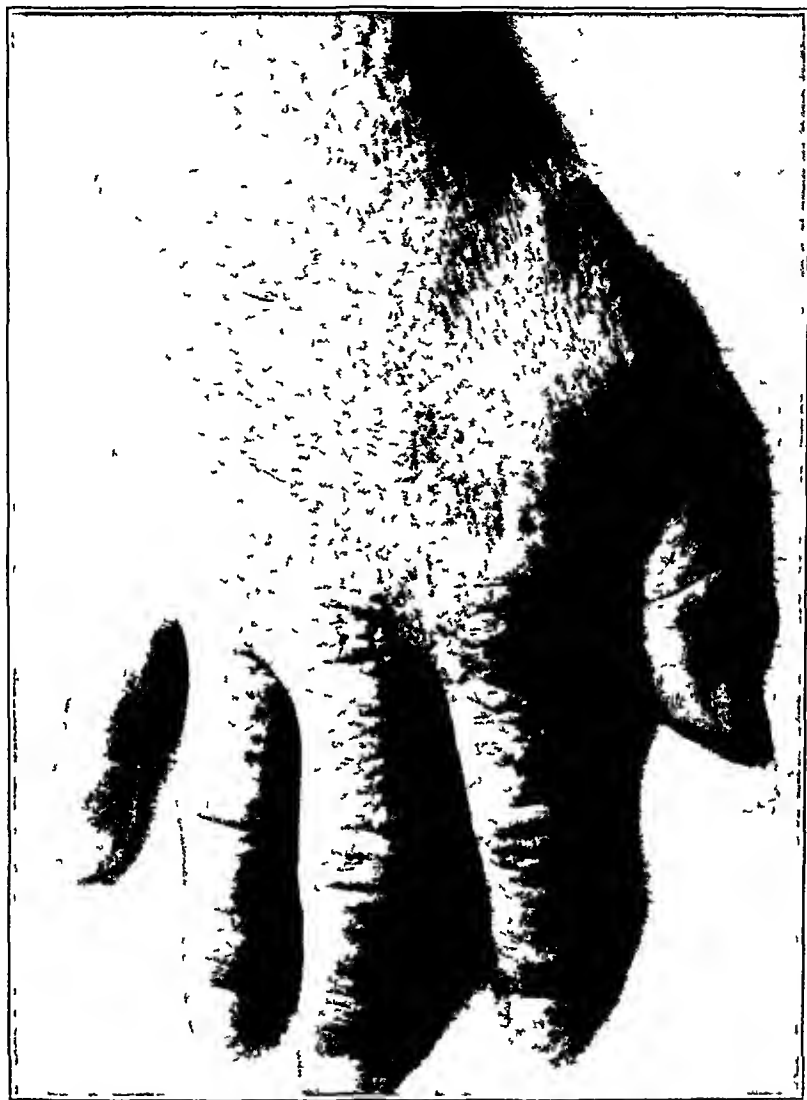


Fig 4—Lichen ruber moniliformis on the right hand

when one presses a finger-tip on a solid rubber ball, the papules imparted a sensation of resiliency but did not feel "shotty." The lesions on the genitals, however, were soft to the touch

On the chest, abdomen, buttocks and genitals the papules were relatively scattered, with normal skin intervening. In other regions, as on the glabella, below the lobes of the ears, on the flexor aspects of the upper extremities, on the backs of the hands and on the external aspects of the thighs, they were closely aggregated but not fused, thus forming a mosaic

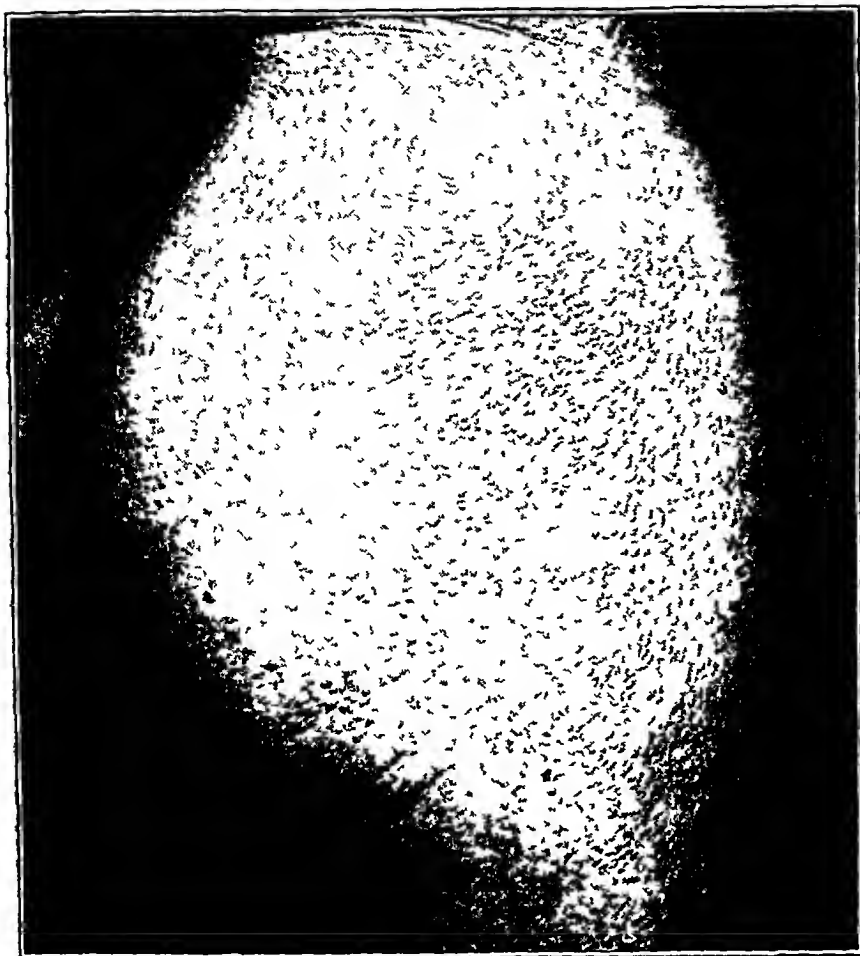


Fig 5—Lichen ruber moniliformis on the right buttock



Fig 6—Lichen ruber moniliformis on the back of the neck

The most prominent moniliform patterns were located on the antecubital areas, the back of the neck at its base, the anterior and posterior axillary folds and the anterolateral aspects of the upper part of the thighs. In the antecubital areas, extending half-way down the forearms and half-way up the arms, the papules gave the impression of having become fused to form fluted narrow keloid-like bands running parallel to the axis of the limb, these bands were most pronounced in the antecubital hollows, gradually shading off toward the less implicated skin on the wrist and middle portion of the arm. These longitudinal keloid-

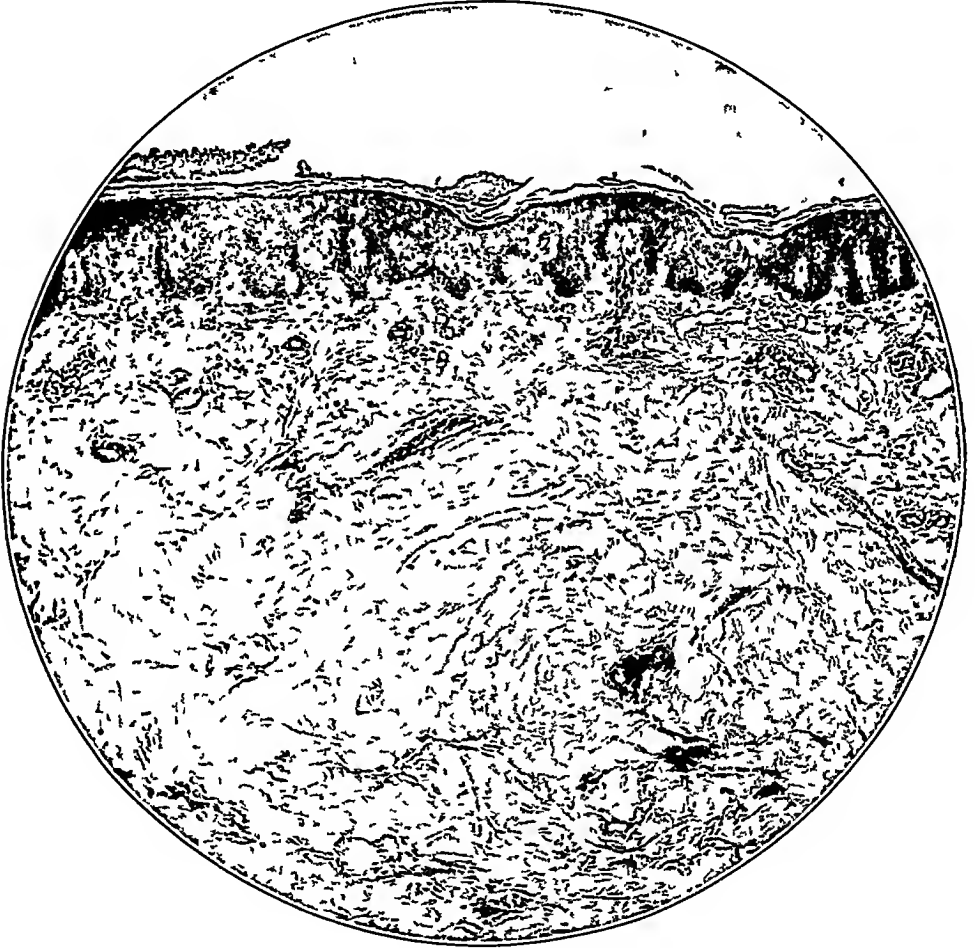


Fig 7—Low magnification of specimen examined on Oct 2, 1935. The active process is predominantly in the upper portion of the cutis, the deeper layers of the cutis show a moderate degree of interstitial and parenchymatous edema.

like strands exhibited more or less well defined cross-hatchings, indicating the lines of contact between the adjacent papules of which the strands were composed. In these areas the red color was of a more dusky hue than elsewhere. In the other regions mentioned as sites of moniliform patterns the beaded arrangement was conspicuous but the keloid-like strands were absent and there was no indication of fusion of the elements or of cross-hatching.

Where the papules were closely aggregated and there were narrow zones of intervening normal skin the appearance of the eruption was suggestive of the surface markings of certain lizards⁹

Subjective symptoms consisted of a moderate degree of itching, especially in warm weather. Marks of scratching were not observed at any time.

Treatment—This was continued diligently over a period of three months and consisted of injections of arsenic in increasing doses, application of filtered and unfiltered roentgen radiation to various parts of the body and different topical

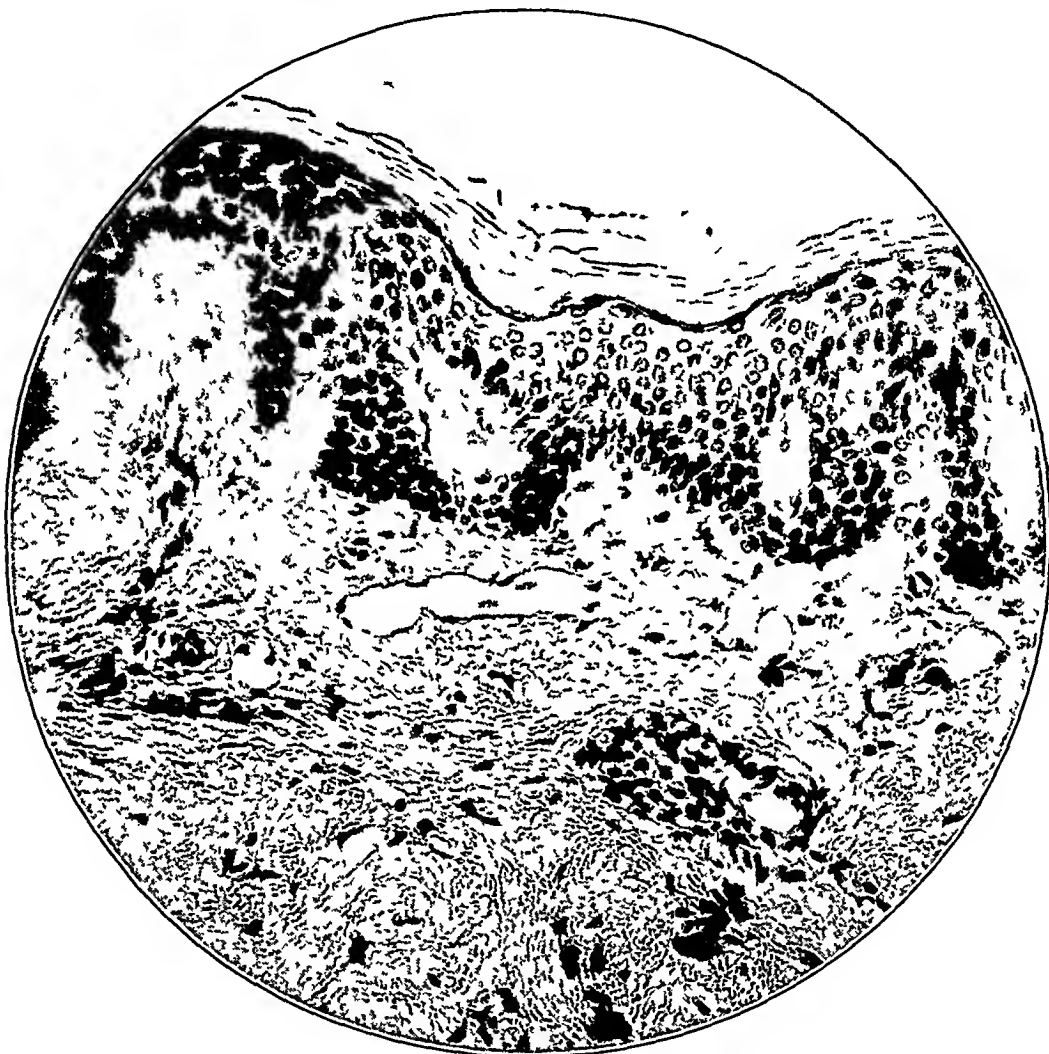


Fig 8—High magnification of part of the section shown in figure 7, showing dilatation of vessels and perivascular lymph spaces and of lymphatics in the upper portion of the cutis and occlusion of some of the vessels and degeneration of vascular walls

applications. The result was disappointing, there was no visible alteration in any of the treated areas, although the patient fortunately had the impression that his eruption showed signs of improvement.

Laboratory Investigations—The routine examinations of the blood and urine revealed no significant deviations from the normal. The Wassermann, Kahn,

⁹ It resembled particularly the appearance of the beaded lizard, known as the Gila monster.

Kline diagnostic and Kline exclusion tests were negative. The blood cell count showed 4,700,000 red cells, 5,200 white cells and 92 per cent hemoglobin. The results of the differential count were as follows: polymorphonuclear leukocytes, 49 per cent, lymphocytes, 43 per cent, monocytes, 1 per cent, eosinophils, 5 per cent, myelocytes, 2 per cent. Chemical examination of the blood gave the following results: urea nitrogen, 9 mg, sugar, 100 mg, cholesterol, 185, and chlorides, 485 mg, per hundred cubic centimeters.

Estimations of the cholesterol content of the blood were made by Dr Isadore Rosen¹⁰. The values obtained and the normal values are given in the following tabulation:

	Patient	Normal
Total lipids, mg per 100 cc	1,660.0	1,510 \pm 91
Total cholesterol, mg per 100 cc	254.0	212 \pm 18
Cholesterol esters, mg per 100 cc	140.0	152 \pm 19
Free cholesterol, mg per 100 cc	114.0	59 \pm 6
Free cholesterol (percentage of total cholesterol)	45.0	28 \pm 4
Lipid phosphorus, mg per 100 cc	7.6	8.1 to 9.6
Albumin, Gm per 100 cc	3.9	4.8 \pm 0.3
Globulin, Gm per 100 cc	2.5	2.6 \pm 0.1

Dopa stains, investigations of amyloid and lipid content of the skin, nerve fiber stain and studies for evidence of infection by bacteria and virus were made by Dr Arthur W. Grace. To ascertain whether the infiltrate contained cells giving a positive reaction to dopa, frozen sections were stained with the dopa reagent by the method of Laidlaw and Blackberg¹¹. No such cells were present in the infiltrate.

Sections covered with paraffin and fixed in solution of formaldehyde were stained by Roger's method for nerve fibers on the assumption that the lesion might represent an unusual type of nevus, as described by Masson¹². No nerve fibers, however, could be demonstrated.

The superficial resemblance of the clinical manifestations to cutaneous amyloidosis prompted a search for amyloid and lipid material in the lesions. Frozen sections were stained with sudan IV, and 0.1 cc of a 1 per cent solution of congo red was injected into a group of lesions. No portion of the sections retained the sudan stain, and the congo red was not absorbed macroscopically by any of the lesions into which it had been injected, in fact, the lesion was apparently less stained by the congo dye than was the surrounding healthy skin. Sections stained with methyl violet did not reveal amyloid in any constituents of the tissue.

10. The total lipid content was determined by extraction with alcohol and ether and by extraction with evaporation in a weighed casserole. The total cholesterol content was determined by a modification of the procedures of Myers and Wardell as described by Krasnow and Rosen (*J Lab & Clin Med* 14:967, 1929), the ester and free cholesterol content, by a modification of the procedures of Bloor and Knudson as described by Rosen, Krasnow and Lyons (*Cholesterol and Lecithin Studies in Syphilis. Cholesterol Partition in Relation to Wassermann Reaction*, *Arch Dermat & Syph* 27:383 [March] 1933), the lecithin content, by the method of Krasnow, Rosen and Porosowska (*J Lab & Clin Med* 20:1090, 1935), and the protein content, by the method of Greenberg (*J Biol Chem* 82:545, 1929).

11. Laidlaw, G. F., and Blackberg, S. N. *Melanoma Studies. II. A Simple Technique for the Dopa Reaction*, *Am J Path* 8:491 (Sept.) 1932.

12. Masson, P. *Les naevi pigmentaires, tumeurs nerveuses*, *Ann d'anat path* 3:417 (May) 1926.

To investigate a possible infectious etiologic agent—bacteria or virus—a group of three papules were excised under sterile conditions and ground up with an amount of sterile physiologic solution of sodium chloride equal to approximately ten times the volume of the excised skin. One portion of the resulting emulsion was incubated at 37 C aerobically in broth of p_H 7.6 containing 0.1 per cent dextrose and a 0.2 per cent solution of di-sodium hydrogen phosphate (Na_2HPO_4 , 12 H_2O). Another portion was incubated anaerobically at 37 C in broth of p_H 7.2 to 7.4 containing calves' liver and 0.5 per cent dextrose. There

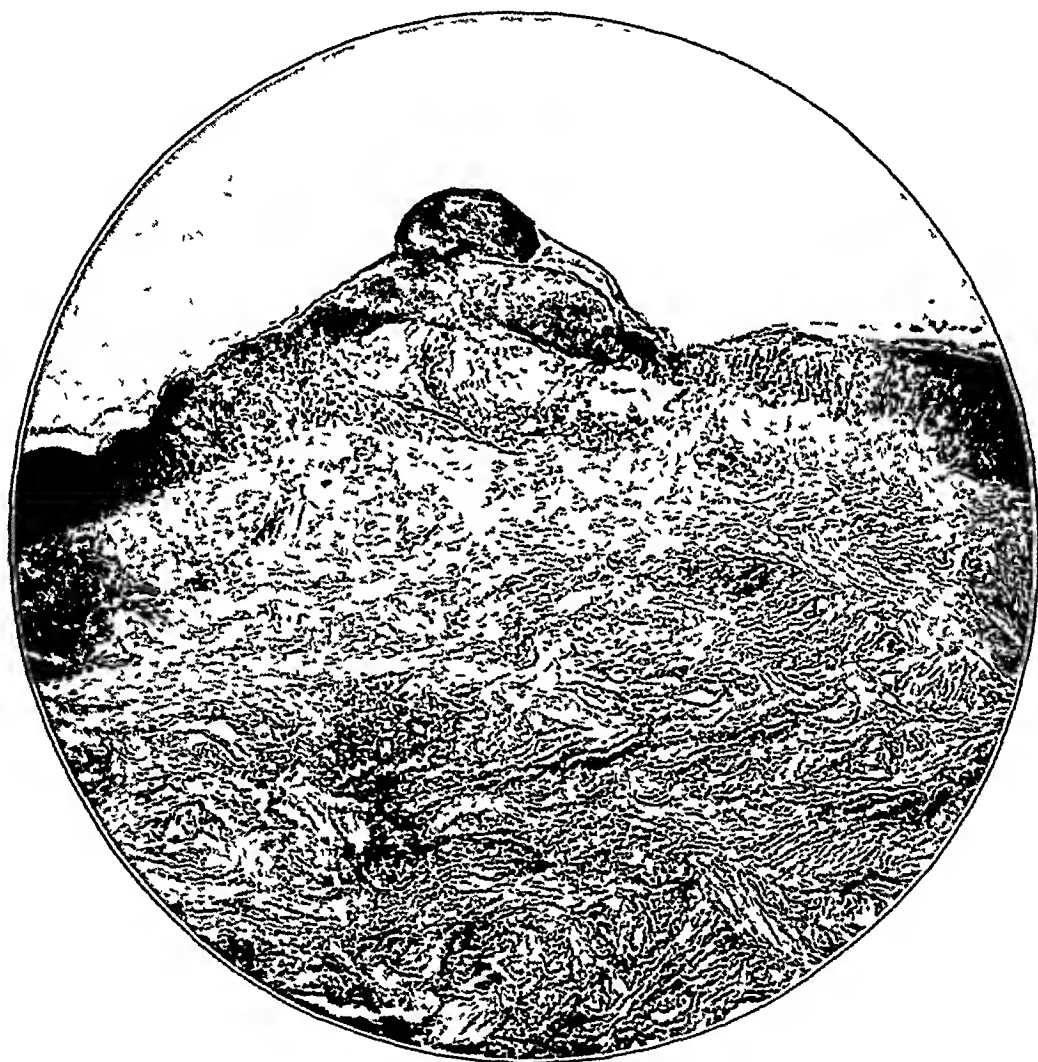


Fig 9—Low magnification of specimen examined on Jan 2, 1936, showing parenchymatous edema and swelling of the cutis involving vessels and perivascular tissues. Granular necrosis of part of the epidermis, resulting in cavity formation with broken-down cellular elements. The middle portion of the cutis shows granular necrosis of the vessel walls, cellular infiltrate and surrounding cutis framework.

was no growth in either medium at the end of one week. Of a third portion 0.1 cc was inoculated intradermally into an unaffected area of skin on the patient's forearm and into a corresponding situation in a normal person. Neither the patient nor the control showed any immediate or late reaction to the inoculation.

HISTOLOGIC OBSERVATIONS

Dr David L. Satenstein¹³ examined several biopsy specimens and reported the results as follows

Biopsy Made on April 3, 1935—The predominant changes were located in scattered areas of the pars papillaris, extending up to the basal cell layer of the epidermis. Two such areas were noted in the section. The remaining portion of the cutis exhibited practically no notable pathologic changes aside from some

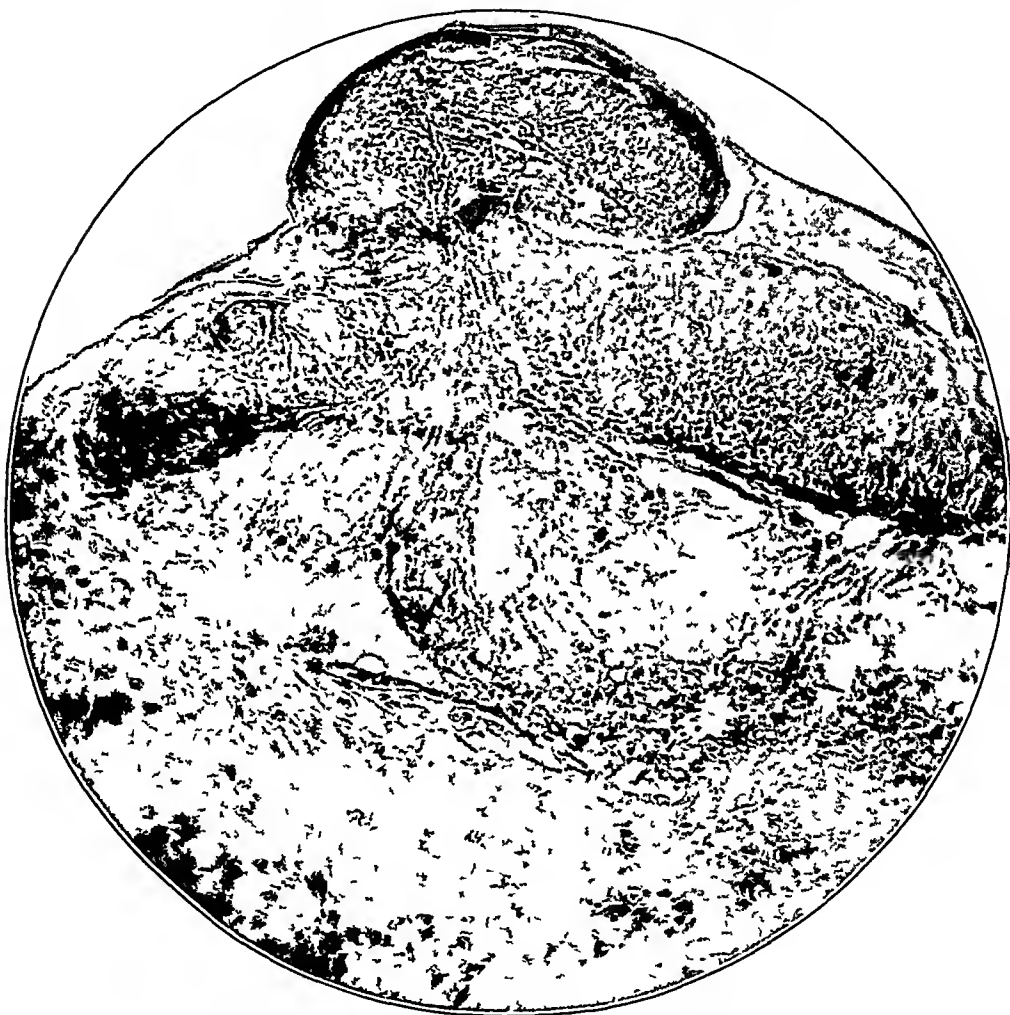


Fig 10—High magnification of section shown in figure 9, showing necrosis and cavity formation

dilatation of the vessels and a few small round cells (lymphocytes) in the perivascular lymph spaces

The epidermis of the entire section except the portion overlying the affected pars papillaris retained its normal general architecture. In the altered areas the

¹³ According to Dr Satenstein the following stains were employed: congo red, sudan IV, hematoxylin and eosin, Roger's nerve stain, methyl violet, dopa and the stains used as a routine for elastic tissue.

basal cell layer was almost completely wanting. The overlying prickly cells were considerably compressed and arranged more or less parallel to the surface, the cell bodies were somewhat indistinct. The granular layer of the entire section consisted of one layer of cells, save in the affected parts, where it was composed of three and four strata. There was a moderate increase in the lamellae of the horn overlying the affected epidermis. There was absence of edema in the epidermis as well as absence of acanthosis, there was no infiltration of any of the contents of the cutis.

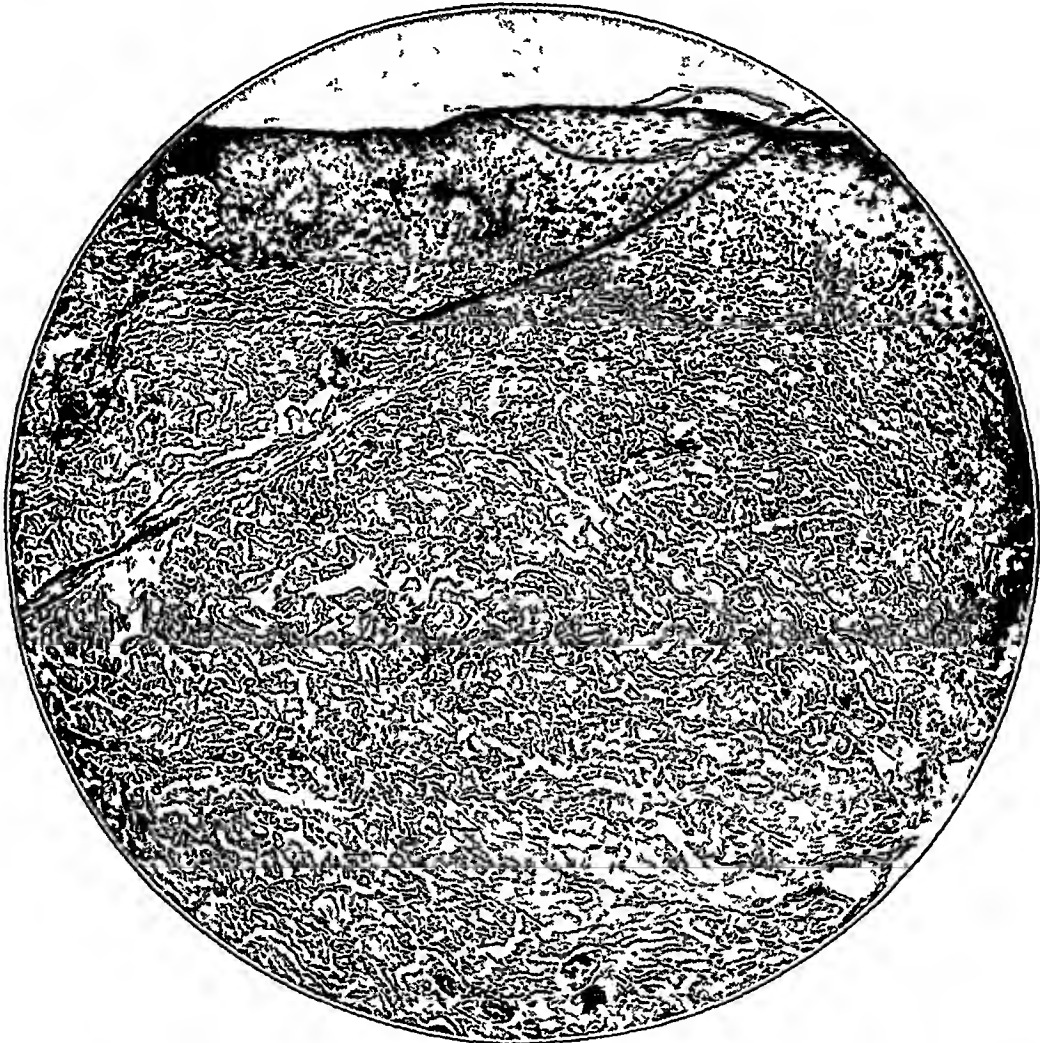


Fig 11—Low magnification of specimen examined on April 3, 1935, showing resting stage or end-stage of some previously active process.

In the pars papillaris, involving approximately three papillary zones, there was a fairly dense cellular mass enmeshed with fine scattered connective tissue fibers but nowhere suggestive of a reticulum. The cells in this area were of the connective tissue variety, with large nuclei, some with and some without nucleoli, there were a few large round cells and some flattened fibroblasts. Below this area were a few fibroblasts fading off into the surrounding cutis. In this area there was an absence of blood vessels, of degenerative changes and of plasma and giant cells.

Resumé The process seemed to depict an end-result or a resting stage of some previously active change. There was nothing in the section to indicate what

the previous picture or process might have been. The impression was that some type of organizing tissue, as is sometimes encountered in the early stages of some of the fibromas, was present.

Biopsy Made on Oct 2, 1935—The active process was predominantly in the upper portion of the cutis, the remaining part presenting a moderate interstitial and parenchymatous edema in the deeper layers, otherwise there were no notable changes.

The overlying epidermis was in part acanthotic and in part normal. There was some fusion of the rete pegs and some broadening but no thinning of the sub-papillary plates. In the basal zone of some of the rete pegs a slight amount of pigment was present, but this was not a uniform observation. The granular layer was everywhere intact and unchanged. The horny layer showed a moderately finely laminated structure. At the orifice of a sweat duct there was an increased amount of compact horny material, filling the orifice completely. There was no evidence of edema of the epidermis and no disturbance or disorganization of the basal cells, and there was absence of elements from the underlying cutis.

In the upper portion of the cutis all the vessels were to some degree dilated, there was a dilatation of the perivascular lymph spaces, which contained a few cellular elements. An occasional dilated capillary was visible within a papillary body. The lymphatics in the upper portion of the cutis were dilated. The walls of some of the vessels were swollen and somewhat homogeneous, suggesting colloid or hyaline degeneration. The nuclei of the lining endothelium projected into the lumen. Some of the vessels were almost completely occluded. In the perivascular lymph spaces were a few small round cells with deeply stained nuclei, and larger somewhat elongated cells with larger nuclei containing somewhat loose chromatin. There were no plasma cells or giant cells. The surrounding cutis presented a considerable number of scattered fibroblasts. A few chorioplaques were noted high up in the cutis. There was absence of disturbance of the elastic tissue, no evidence of degeneration or necrosis of either the connective tissue or the cellular elements was noted.

Resume The process consisted of a moderate exudative inflammatory change which had probably undergone a slow development, it had not advanced to a great extent, remaining superficial and resulting in a degeneration of the vessel walls. The entire picture was not of sufficient intensity to be interpreted as characteristic of any orthodox dermatosis.

Biopsy Made on Nov 25, 1935 (Osmic Acid Stain)—This section lacked informative material. Minute droplets taking the black dye were scattered throughout parts of the epidermis, scattered larger droplets were seen in the deep layers of the cutis.

Resume There was absence of lipoidosis aside from what is normally encountered.

Biopsy Made on Jan 2, 1936—The active process extended through the entire cutis as well as into portions of the epidermis. Owing to parenchymatous edema the entire cutis was markedly swollen. The vessels and perivascular tissues were predominantly affected, although other areas of the cutis were involved to a lesser degree. Over one half of the section the overlying epidermis was considerably flattened and somewhat hypertrophied. The central portion of the section, occupying an area of about a half-dozen papillae, exhibited an almost complete granular necrosis of the epidermis resulting in the formation of a cavity containing broken-down cellular elements. In the epidermis surrounding this area there was a considerable degree of degeneration of some of the epidermal cells, causing a loss

of cellular outline. Immediately below this cavity, forming its floor, the cutis showed signs of degenerative changes. The walls of the vessels, especially in the middle and upper portions of the cutis, were swollen and somewhat homogeneous, and contained numerous broken-down cellular elements, the lumens in some were completely occluded, in others they were still visible, being lined with swollen endothelium. In the perivascular lymph zones were closely packed broken-down cells. Similar cellular detritus was noted lying between bundles of swollen connective tissue in the perivascular zones. Some of these bundles were finely granular.

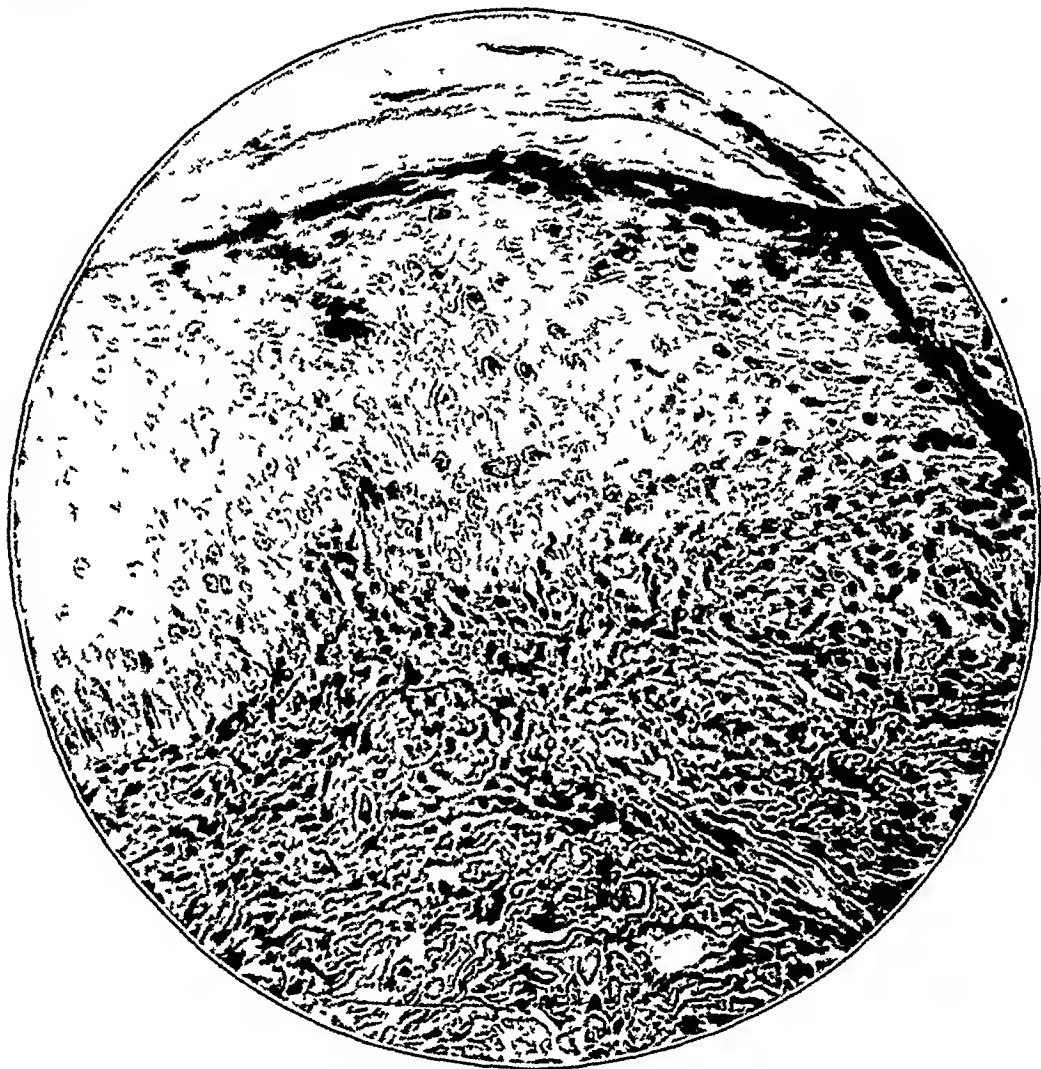


Fig 12—High magnification of section shown in figure 11

In the deeper portions of the cutis some proliferation of fibroblasts was seen. In the subepidermal zone the cellular infiltration was composed predominantly of lymphocytes, here the greater portion of the cutis was homogeneous and had lost its characteristic structure.

The sweat glands exhibited a high grade of so-called cloudy swelling of the lining cells with some hyaline degeneration of their connective tissue coats. In one of the sebaceous glands fragmentation of the cells was noted and considerable cellular detritus surrounded the gland.

Résumé In this section the entire histologic picture was one of rather profound degeneration and disintegration of the walls of the vessels, the cellular

infiltrate and the framework of the cutis. It was suggestive of a necrotic dermatitis involving especially the vascular elements.

The section did not exhibit changes tending to indicate etiologic or pathogenic factors or to correlate the histologic observations with the clinical-morphologic picture.

Summary of Histologic Observations—From the histologic study of four pieces of tissue removed from different parts of the body and examined, respectively, on April 3, 1935, Oct. 2, 1935, Nov. 25, 1935, and Jan. 2, 1936, it is not possible in the light of the chronologic sequence indicated to visualize the pathologic process. However, a rearrangement of the specimens makes such a visualization feasible.

The specimen examined on Oct. 2, 1935, indicated the early stage of the pathologic process, namely, one consisting of an exudative inflammatory reaction in the upper portion of the cutis associated with a degeneration of the vessel walls but as yet no necrosis of any of the tissues or of infiltrative elements.

The last section, examined on Jan. 2, 1936, evidently showed the process at its height, as indicated by intense degeneration and disintegration of tissue and of cellular infiltrate as well.

The first section, examined on April 3, 1935, presented the final stage of the process, i. e., the deposition of connective tissue cells—possibly organizing tissue—replacing the parts which had broken down.

There were no changes in the specimens which would lead one to link the pathologic picture with any form of the so-called lichens.

The process was evidently one in which vascular disease associated with degenerative changes was the predominant morbid alteration.

SUMMARY AND CONCLUSIONS

By a process of elimination the compilation and perusal of the cases recorded as instances of lichen ruber moniliformis leaves only two instances in which microscopic examination definitely excludes lichen planus, namely, Kaposi's and our case. The similarity of clinical manifestations in these two cases and the obvious dissimilarity of the picture to that in cases in which microscopic examination revealed lichen planus seem to support the contention of the critics who regard the original "lichen ruber moniliformis" not only as a dermatosis unrelated to lichen planus but possibly as one which might prove to be a disease sui generis. The histologic changes in our case would at least lead one to accept this point of view.

The points of resemblance between Kaposi's and our case may be summed up as follows. There is a close parallelism in the distribution of the lesions, their morphologic features, their multiformity, their variations in color, size and arrangement, the absence of marks of scratching, the chronicity, the similarity of some elements to papules of lichen planus and finally, the lack of discoverable etiologic and pathogenetic features. On the other hand, the dermatosis in Kaposi's case differs from that in ours in that the longitudinal banded keloid-like formations on the neck and extremities were far more pronounced and much more

prominent in his case than in ours, in his case there were central depressions in some of the papular elements, lesions of the labial and buccal mucosa, a retiform design of papular chains on the thighs, longitudinal bands on the lower portion of the abdomen and a scattering of pigmented puncta in the midst of the other lesions. Judging from his description the buccal manifestations possessed none of the diagnostic features of lichen planus. In neither case was the glans penis involved.

Regarded from a broad point of view it might be assumed that the dermatosis in Kaposi's case was a manifestation of a much further advanced phase of development and evolution than that which obtained in our patient. This point of view is, of course, a purely conjectural one, especially when one considers the great discrepancies in the respective microscopic structural features.

We are concerned with a dermatosis the character of which appears to be in certain respects unique. Since dermatologic literature abounds in new and often confusing names, it behooves one to restrain the creative impulse and to avoid as much as possible further derangements of nomenclature. Nevertheless, a different name seems desirable, and the new name should preferably be one which would serve to maintain a plausible harmony with the original. Taking into consideration the clinical similarity of the dermatosis exhibited by our patient to that described by Kaposi, its nonrelation to lichen planus, the lack of etiologic and pathogenic clues to its identity and, finally, the desirability of not insulating it from Kaposi's designation, we have selected for the dermatosis the neutral name *morbus moniliformis lichenoides*.

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ABSTRACT OF DISCUSSION

DR F M JACOB, Pittsburgh. As the authors have stated, a review of the literature, particularly of the textbooks, shows the general belief to be that lesions of lichen ruber moniliformis are not often found in association with lichen planus. This is easily understood because clinically lesions that are found occasionally in association with lichen planus are similar to the individual lesions described in this case.

I recently observed a case of what appeared to be clinically a beginning of lichen ruber moniliformis, there were waxy yellowish lesions about 3 mm in diameter on the arms and wrists, deep-seated domed lesions that had no resemblance to clinical lichen planus but histologically showed a definite picture of lichen planus and no characteristics that could be compared to the ones in Dr Wise and Dr Rein's case.

There are several diseases previously described that have some similarities to this, namely, some of the diseases that appear under the description of scleroderma, lichen sclerosus et atrophicus, lichen morphoeicus atrophicus and dermatitis lichenoides chronica atrophicans. Montgomery and Ormsby differentiated between white spot disease and lichen sclerosus some time ago, and in their cases of lichen

sclerosus there were some histologic features that were similar to those in the case reported by Dr Wise and Dr Rein. Wise and Shelmire in a paper on dermatitis lichenoides chronica atrophicans also showed some histologic similarities to the disorder under consideration. In writing both papers Dr Wise was able to stress the differential points.

Satenstein in the same way has stressed the differential points between lichen ruber moniliformis and these other diseases with particular regard to the pigmentation, the formation of reticulum, the character of the exudate and the final connective tissue reaction which was present in Dr Wise and Dr Rein's case.

The one particular feature, however, that is found to be similar in all the aforementioned conditions is the changes in the deeper blood vessels, consisting first of swelling and later of proliferation of the endothelial lining of the blood vessels, leading to occlusion of these vessels. This suggests some deep-seated toxic process that may be similar in all of these conditions.

In spite of the fact that the nomenclature is rather overcrowded, I think it is not amiss to give this disease the descriptive name Dr Wise and Dr Rein have suggested in order that it be differentiated from lichen planus until its nature is ascertained.

DR HAMILTON MONTGOMERY, Rochester, Minn. Dr Wise and Dr Rein are to be complimented on the thoroughness with which they studied their case, especially as to the ruling out of such changes as deposition of lipoid and amyloid. The histologic picture is unlike any I have seen before. The disorder obviously is not lichen planus and does not fit in with the picture of scleroderma, lichen sclerosus et atrophicus or morphoea guttata. It is difficult to explain the necrosis present in the fully developed lesion, especially since, as I understand, it was not apparent clinically.

I want to call attention to Dr Ormsby's case, in which, I understand, the disorder has persisted over a period of about twenty years and has not responded to treatment. The latter is true of Dr Wise and Dr Rein's case. This, together with the unusual picture, suggests that the condition may be a nevoid vascular disturbance of some kind, the term nevus being used in the broad sense.

DR L. H. WINER, Minneapolis, Minn. I did not think that the picture in the slide shown resembled lichen planus at all, and I agree with Dr Montgomery that it does not resemble a lichenoid scleroderma. Still, at the termination of the process the lesions healed with relative increase of the connective tissue, and therefore my impression is that this condition eventually will be more closely related to the sclerodermas or the tense atrophies than to lichen planus.

DR FRED D. WEIDMAN, Philadelphia. This paper is of value from two points of view: (1) from the clinical one involving nomenclature, with its bearing on erudite dermatologic diagnosis and general clinical dermatology, and (2) in relation to the etiology. However, I think that the more valuable feature of this presentation is in relation to the latter aspect, the clinical circumstance that these nodules, at least in part, tend to extend in strands makes one think of some particular anatomic structure in the skin, and since these lesions appear most conspicuously at the flexures of the elbows, the lines of fibrous overgrowth that appear in connection with stress and strain seem to be important.

Thus, it is well known (English authors discuss this more than American authors) that among the various expressions of rheumatism there is a lesion which is called fibrositis, it is a nonspecific type of fibrous reaction. After joining up what has been shown here clinically, namely, the pattern of the lesions on the skin, with what has been demonstrated histologically, I think that attention ought to turn toward the possibility of a diffuse generalized toxic state which is analo-

gous to rheumatism I suggest as the most promising line for studies in the etiology of this disease cultures of the blood and examination of the economy at large for foci of infection

Such a wealth of information would not have been available had Dr Wise and Dr Rein limited their study to but one or two biopsies But eleven biopsies were made Only in that way were the authors able to find one lesion which fortunately happened to show the acute and more informative phases of the fundamental pathologic process

DR CHARLES R REIN, New York I wish to call attention to the two cases reported in this country, one by Fox and the other by Hyde and Ormsby, which were the only ones in which the disorder closely resembled that in our case Unfortunately, however, tissue for microscopic examination was not obtained in these cases

Regarding Dr Weidman's discussion, I wish to state that our patient was carefully examined for foci of infection, the results of the various examinations gave essentially negative results

PSEUDO-ACHROMIA OF TINEA VERSICOLOR

CLINICAL AND EXPERIMENTAL STUDIES AND OBSERVATIONS ON
THE USE OF FILTERED ULTRAVIOLET RAYS
(WOOD FILTER)

GEORGE M LEWIS, M D

AND

MARY E HOPPER, M S

NEW YORK

A patient with tinea versicolor not uncommonly exhibits during the summer or autumn light-colored (apparently depigmented) areas on the surfaces of skin exposed to sunlight. These areas usually appear suddenly, after sunburn followed by peeling, although a history of a visible reaction is not always obtained. The patches occupy the sites of lesions of tinea versicolor, being irregular and of various size, and appear chiefly on the trunk. Their color is not the dead white of vitiligo, although in contrast to the surrounding skin, especially in persons of dark complexion, they may be mistaken for that disease. Other areas of skin on the covered parts of the body are usually found to match the color of the achromic-appearing spots. There is no increase of pigment at the periphery of the lesions. A scarcely perceptible scaling may be noted. Sometimes the condition appears year after year, becoming less noticeable during the winter and reappearing during the summer. This manifestation of tinea versicolor was first described by Ehrmann¹ and has been studied by Wertheim,² Kistiakovsky,³ Gougerot, Joyeux and Arnaudet,⁴ Artom,⁵ del Vivo,⁶ Ruete⁷ and others.

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1 Ehrmann, cited by Wertheim²

2 Wertheim, L. Ueber Lichtwirkung und Leukoderma bei Pityriasis versicolor, *Dermat Ztschr* 38 343 (June) 1923

3 Kistiakovsky, E. V. (a) Pityriasis Versicolor and Ultraviolet Rays, *Arch Dermat & Syph* 15 685 (June) 1927, (b) L'achromie, qui apparaît sous l'action des rayons ultra-violet du soleil sur le pityriasis versicolor, est-elle parasitaire ou post-parasitaire? *Ann de dermat et syph* 1 1264 (Dec) 1930

4 Gougerot, Joyeux and Arnaudet. Un cas d'achromie parasitaire nord africain, *Bull Soc franç de dermat et syph* 37 110 (Jan) 1930

5 Artom, M. Contributo allo studio della pityriasis versicolor acromizzante, *Gior ital di dermat e sif* 71 1945 (Dec) 1930

6 del Vivo, G. Sulla così detta pityriasis versicolor acromizzante, *Rinasc med* 9 270 (June 15) 1932

7 Ruete, A. E. Zur Frage der depigmentierenden Pityriasis versicolor, *Dermat Wchnschr* 96 333 (March 11) 1933

The light-colored areas do not, as a rule, become tanned after further exposure to ultraviolet radiation, on the contrary, they become more and more noticeable owing to the increase of pigment in the surrounding normal skin. The condition has been said to occur in the skin of Negroes in association with the development of definite depigmentation. The development of lesions on covered parts of the body which have not been sunburned has been reported. Furthermore, the dopa reaction has demonstrated that the pigment-forming oxidase may be affected. For these reasons it has been suggested that the light-colored areas may be due to a toxic action of the fungi on the pigment of the skin resulting in an inhibition or destruction of the pigmentary powers of the skin. The rôle of the sun in activating the fungi is not clear. The explanation for the persistence of the light-colored areas, namely, that the fungi in the lesions of tinea versicolor act as a mat or filter to prevent the ultraviolet rays from the sun from passing through, is held by many observers.

DIFFERENTIAL DIAGNOSIS

Certain other diseases with similar clinical pictures must be considered in a differential diagnosis from the pseudo-achromia of tinea versicolor. Among these may be mentioned *achromie parasitaire à récurrence estivale* (Jeanselme), *achromia parasitaria* (Pardo-Castello and Dominguez), *tinea flava* (Castellani), the endemic vitiligo of Turkestan (Minch) and *pinta* in the quiescent stage. Besides post-eruptional depigmentations, the condition may also be confused with syphilitic leukoderma and with ordinary vitiligo.

1 *Achromie parasitaire à récurrence estivale*—From the published description⁸ it appears that this is the same disease as the one under consideration in this paper.

2 *Achromia parasitaria*—It is difficult to fit together the varied symptoms in the syndrome which Pardo-Castello and Dominguez⁹ described. In some cases of *achromia parasitaria* irregular dirty white macules and patches with slight inflammation, which are scaly and somewhat itchy, are present on the face and neck. In other cases the eruption is generalized, no inflammatory symptoms are present and the disorder simulates the pseudo-achromia of tinea versicolor. On one of the illustrations in the article by Pardo-Castello and Dominguez are shown lesions on the trunk which are suggestive of the disease under discussion in this report. In both disorders the scaling in the early macules is white and furfuraceous, and the older lesions are devoid of scales.

⁸ Jeanselme. Cours de dermatologie exotique. *Achromie parasitaire de la face et du cou, à récurrence estivale*, Paris, Masson & Cie, 1904, p. 239.

⁹ Pardo-Castello, V., and Dominguez, M. *Achromia Parasitaria*, Arch Dermat & Syph 9:82 (Jan) 1924.

There is no increase of pigment at the edges. The mucous membranes, hair and nails are not affected. In the series reported by Pardo-Castello and Dominguez there were four cases in which the disorder was generalized, the palms and soles being free. *Aspergillus* was cultured in six of thirty-six cases and was considered a possible cause of the disease. No mention was made of the examination of scales in potassium hydroxide for the presence of *Microsporon furfur*. In a later communication Pardo-Castello¹⁰ expressed his belief that the same clinical picture might be found in patients of different races and in persons residing in different countries, that it might affect different types of persons and that it might be caused by a variety of organisms. He did not believe that the rays of the sun play any part in the etiology. Further investigative work appears necessary to clarify the picture.

3 *Tinea Flava* or *Tinea Versicolor Tropicalis*—Castellani¹¹ stated that this condition is identical with achromia parasitaria (Pardo-Castello and Dominguez). The fungus responsible cannot be distinguished from *M. furfur* in potassium hydroxide preparations and, like that organism, is nonculturable. Castellani¹² differentiated *tinea flava* from *tinea versicolor* as it occurs in the temperate zones by the following points: (1) *tinea flava* begins in childhood and may persist during life, (2) it usually affects the exposed parts of the body, (3) cure is difficult, and (4) the fungus seems to have a marked depigmentary action.

4 *Endemic Vitiligo of Turkestan*—According to Kistiakovsky,^{3a} who has observed the disease, there is no difference between this disorder and vitiligo.

5 *Pinta*—When this condition is observed early, the characteristic hues of the affected skin in no way suggest *tinea versicolor*. Later, when vitiliginous areas are present, the differentiation may be more difficult. The disease causes coarse scales, the affected skin is infiltrated, occasional fissuring is noted and loss of hair is usual. When extensively involved, the skin presents an odd piebald appearance.

6 *Syphilitic Leukoderma*—This condition is seen almost exclusively in women. The lesions are commonly symmetrically located on the sides of the neck, are oval or irregularly shaped and vary from the size of a split pea to that of a dime. Concomitant hyperpigmentation is some-

10 Pardo-Castello, V. *Achromia Parasitaria. Its True Nature and Etiology*, Arch Dermat & Syph 25 785 (May) 1932.

11 Castellani, A. *Fungi and Fungous Diseases*, Arch Dermat & Syph 17 194 (Feb) 1928.

12 Castellani, A. *A Case of Pityriasis Versicolor Tropicalis*, Brit J Dermat 47 484 (Nov) 1935.

times noted. No scaling is present. Other evidence of syphilis may usually be detected, including a positive serologic reaction.

7 *Vitiligo*—The irregular, asymmetrical, snow-white patches, affecting by preference the face, hands, forearms and male genitalia and showing hyperpigmented edges, should not often prove difficult to differentiate. No scaling is present. The appearance of vitiliginous skin when observed under filtered ultraviolet rays is characteristic, presenting a fluorescing, glistening white color.

8 *Posteruptional Depigmentations*—Seemingly-depigmented areas may be noted at the former sites of syphilitic, psoriatic and other cutaneous lesions. Without any history of a preceding eruption the differential diagnosis may be difficult.

Comment—Since cases occur in which a clinical diagnosis may be impossible, it is considered not only desirable but necessary to make a positive diagnosis in all cases of pseudo-achromia due to tinea versicolor by means of microscopic studies reinforced by observations with filtered ultraviolet rays.

REVIEW OF RECENT LITERATURE

Kistiakovsky^{3a} thought that in many of Pardo-Castello's patients, especially in those with lesions on the back, the picture resembled that of pseudo-achromia of tinea versicolor in patients he had observed. He ascribed the light coloration of the skin to a mechanical screening of the skin underlying the patch of tinea versicolor and pointed out that *M. furfur* contains a yellowish pigment which strongly refracts light. Because of this property of the organism parts of the skin covered by fungus were not sunburned. He did not agree with Stein, who thought that a special kind of *M. furfur* was responsible for the condition. Gougerot, Joyeux and Arnaudet⁴ and Artom⁵ considered the light areas to be a true achromia and not pseudo-achromia due to the contrast between the normal and the surrounding skin. Kistiakovsky,^{3b} in a later report, reiterated the view which he had expressed earlier and stated that in all parasitic diseases with an achromic aspect the mechanism of origin is physical and not biologic. Del Vivo⁶ reported a case of a disorder which he considered pseudo-achromic. In commenting on this report, Wise and Sulzberger¹³ stated that in certain cases of tinea versicolor it is likely that there is a true depigmentation of the skin. They based their belief on several cases in Negroes in which they saw lighter patches of skin become much lighter and contain less pigment than the normal, not sunburned, areas. Ruete⁷ expressed the belief that the depigmentation is the result of a biologic phenomenon. In the case he reported the patient had typical tinea versicolor. The brown

13 Wise, F., and Sulzberger, M. B. *The Year Book of Dermatology and Syphilology*, Chicago, Year Book Publishers, Inc., 1932, p. 29.

spots turned white but became brown again in the winter. The next summer they again turned white. In a section it was demonstrated that pigment was absent below the areas infected with the fungus. Sections stained by Gram's method and the dopa reaction pointed to a true depigmentation. Cases of apparent achromia in patients with tinea versicolor have been reported in the United States by Fox,¹⁴ MacKee,¹⁵ Throne,¹⁶ Barney,¹⁷ Lewis¹⁸ and Bechet.¹⁹

PERSONAL OBSERVATIONS

We have studied fourteen cases²⁰ of tinea versicolor in which an apparent depigmentation was noted. Repeated examinations for fungi combined with observation of the patients under filtered ultraviolet rays revealed that organisms were frequently present in these light-colored patches. Treatment was continued until no fungi could be demonstrated. Ultraviolet radiation was then given, resulting in an increase of color in the patches.

CASE 1—S. R., a blond woman aged 20, single, an embroidery worker, was presented before the Section of Dermatology and Syphilis of the New York Academy of Medicine in November 1934.¹⁸ Patchy areas of apparent depigmentation on the chest and arms corresponded in color to that of the face and neck. A typical brownish patch of tinea versicolor was present on the back. *M. furfur* was found in scrapings from the lighter areas on the arms and from the brown area on the back. Topical treatment consisting of application of a saturated solution of sodium thiosulfate was continued for three weeks, until there was no evidence of fungi. The patient then received several treatments with artificial sunlight, and within a month pigment had increased in all the pseudo-achromic areas.

CASE 2—A. F., a woman aged 27, a switchboard operator, showed typical patches of tinea versicolor and numerous areas of apparent depigmentation varying in size on the upper portion of the back. Scaling was noted in these lighter areas. Light brown fluorescence was noted in both the lighter and the darker patches when the areas were examined under filtered ultraviolet rays. *M. furfur*

14 Fox, H. *Pityriasis Versicolor Followed by Apparent Depigmentation*, *Arch Dermat & Syph* **15** 751 (June) 1927

15 MacKee, G. M., in discussion on Fox¹⁴

16 Throne, B. *Achromia Cutis Postparasitaria*, *Arch Dermat & Syph* **18** 146 (July) 1928

17 Barney, R. E. *Pseudo-Achromia Postparasitaria—Tinea Versicolor*, *Arch Dermat & Syph* **25**:1167 (June) 1932

18 Lewis, G. M. *Tinea Versicolor (White)*, *Arch Dermat & Syph* **31** 911 (June) 1935

19 Bechet, P. *Vitiligo? Tinea Versicolor?* *Arch Dermat & Syph* **32** 960 (Dec) 1935

20 Twelve cases were observed in the service of Dr. Fred Wise in the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, and two cases were observed in private practice.

was demonstrated in scrapings taken from both types of patches. Local treatment was continued for one month. The patient then received three erythema doses of ultraviolet rays at weekly intervals, and the normal color of her skin returned.

CASE 3—R. W., a man aged 23, married, a clerk, had whitish patches of various sizes on his trunk and several typical areas of tinea versicolor on the sides of his neck and trunk. Examination revealed fungi in the brown areas; no fungus was found in the whitish patches. Topical treatment was instituted for three weeks. At the end of that period examination for tinea gave negative results in all the areas. Two treatments with ultraviolet rays brought back

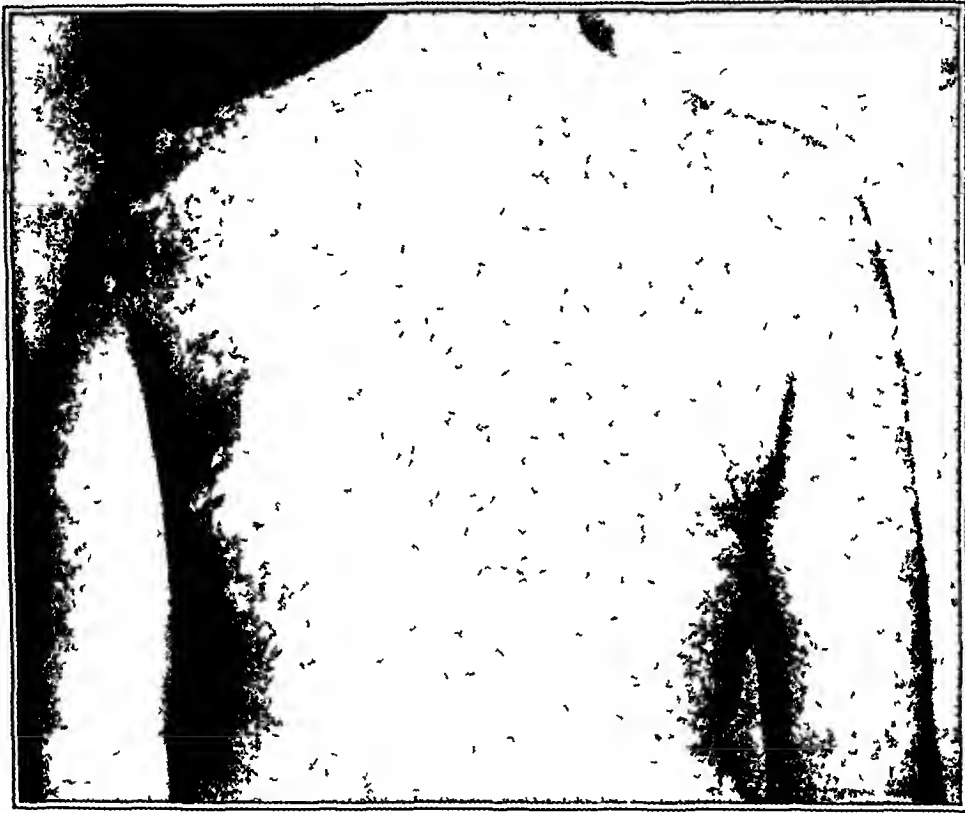


Fig 1—Apparent depigmentation at the sites of lesions of tinea versicolor following an acute sunburn. *M. furfur* was found in scales from several lesions.

some color in the apparently depigmented areas. The patient was not observed further.

CASE 4—V. S., a woman aged 21, single, had numerous coin-sized roundish "depigmented" patches on the upper portion of the back, these were said to have been present for several months. No brown patches were noted. Examination of scrapings from the lighter areas revealed *M. furfur*. Local treatment was instituted, and four weeks later the examination for tinea gave negative results. One treatment with ultraviolet rays was given, but the result was not ascertained.

The development of pseudo-achromic patches was observed to appear at the sites of tinea versicolor. These light areas had not been present when the patient was previously seen.

CASE 5—J G, a woman aged 30, when first seen had scaly fawn-colored patches on her back. The examination revealed *M furfur*. The patient did not use the local treatment prescribed. When she was observed two weeks later, after she had suffered acute sunburn several times, the sites of the eruption showed less pigmentation than the surrounding skin. The color in these areas was not vitiliginous but rather that of normal skin not reached by the sun. Scaling was still present in the areas, and the examination for fungi and the fluorescence test gave positive results. The patient did not return for further study.



Fig 2—Characteristic light-colored areas. *M furfur* was demonstrated in scales from these lesions.

The observation of *tinea versicolor* under filtered ultraviolet rays is useful not only as a diagnostic aid but also in determining the extent of the eruption. Lesions not visible in ordinary daylight fluoresce with the golden brown color typical of the ordinary patches.

CASE 6—P B, a woman aged 23, single, a clerk, had typical patches of *tinea versicolor* on her chest. Under filtered ultraviolet rays additional fluorescent areas (not visible in daylight) were noted on the back of the neck, across the shoulders and on the outer aspect of the anterior portion of the forearm and arm. No local treatment was prescribed. The patient received sufficient sunburn at a

LEWIS-HOPPER—TINEA VERSICOLOR

beach so that all areas of tinea versicolor, the visible as well as the invisible ones, were exfoliated. One week later there was a definite lightness at the sites of the patches of tinea versicolor, as compared to the surrounding skin. M. furfur could still be demonstrated, and fluorescence was still noted. Topical treatment was instituted, and in two weeks no evidence of fungi could be detected. Further exposure to the sun then resulted in an increase of pigment in the light-colored patches.



Fig 3—Small and large areas of pseudo-achromia, which showed the fluorescence characteristic of tinea versicolor when examined under ultraviolet rays and from which M. furfur was recovered.

CASE 7—G. K., a woman aged 28, single, a dress finisher, had a typical eruption of tinea versicolor on the trunk for over two years. Her skin had not been exposed to the sun, and there were no areas of apparent depigmentation. The examination for fungi revealed M. furfur. Examination with filtered ultraviolet rays disclosed several additional areas not noted in ordinary light (fig 4). The patient was not observed further.

MYCOLOGIC EXAMINATION OF THE PSEUDO-ACHROMIC AREAS

The microscopic appearance of the fungi present in the light-colored areas varied somewhat from the picture in a typical patch of tinea versicolor. Few spores were noted, and there was no appreciable grouping. The filaments were few and consisted of short rods.

USE OF FILTERED ULTRAVIOLET RAYS

The well known golden yellow or brown fluorescence noted when lesions of tinea versicolor are examined with filtered ultraviolet rays

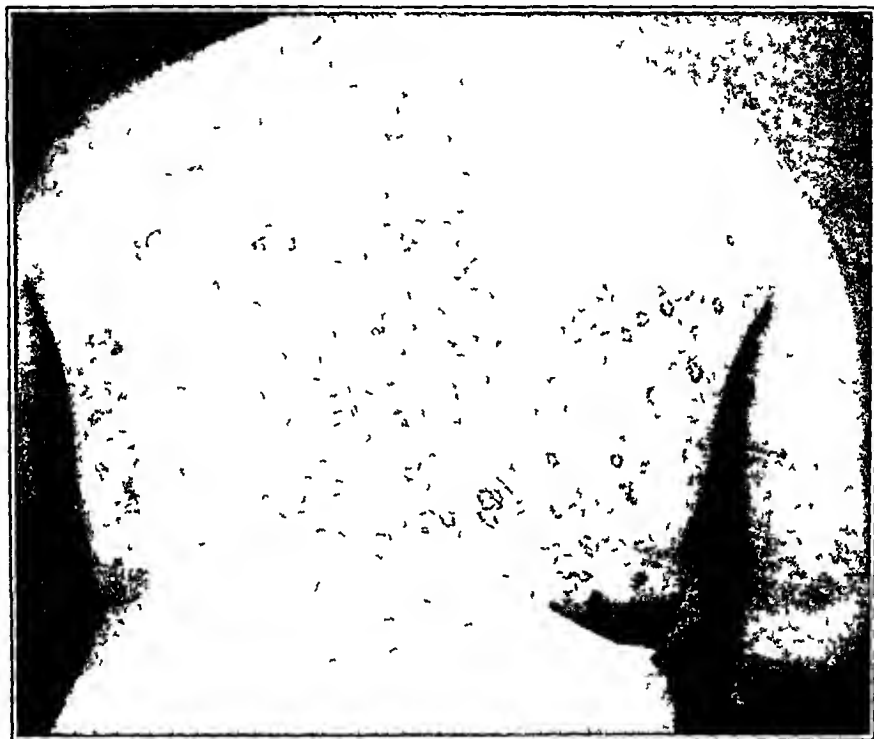


Fig 4 (case 7)—Photograph of lesions of tinea versicolor as seen under filtered ultraviolet ray and outlined in ink. These lesions were not visible in ordinary daylight.

has made such examination a useful diagnostic procedure for many years. The color has varied in different cases from a light brown or yellowish color to a dark brown. The difference in color appears to depend on the amount of pigment in the patch, so that in lesions of tinea versicolor which are quite dark the fluorescent color is also dark. The production of this pigment appears to have some relation to stimulation due to the sun's rays, since the patches may be so light as to be almost invisible during the winter and assume a much darker hue during the period of exposure to insolation. The light-colored areas, which may

be almost invisible to the naked eye, fluoresce brilliantly. It is suggested that the frequent recurrence of tinea versicolor may be due, in part at least, to these practically invisible areas, which provide a focus for dissemination during the summer. So far as the light-colored (pseudo-achromic) areas are concerned, a light brown fluorescence is noted under filtered ultraviolet rays as long as fungi may be demonstrated in scrapings from these areas. When no further fungi can be detected, the color is dull white (in contrast to the brilliant white of vitiligo). The distribution of tinea versicolor may be quickly and accurately determined in any given case by examining the patient with filtered ultraviolet rays. It was found that lesions of tinea versicolor usually occurred on the areas of the trunk on which seborrhea usually develops, but the back of the neck and the extensor surfaces of the arms were not uncommon sites. In two instances lesions were present on the face, and in one lesions were observed in the pubic region. In no case was a patch of tinea versicolor noted on the lower extremities. The scalp was similarly free.

NATURE OF THE LIGHT-COLORED (PSEUDO-ACHROMIC) AREAS

It appears logical to conclude that in the fourteen cases of tinea versicolor which we studied and in which a light-colored area of skin was also present a mechanical and not a biologic factor was responsible for the light color. In some instances, particularly in the case of patients with dark skin, the light-colored areas appeared achromic. Further observation usually made it possible to match the color of the light-colored patches with other areas of the patient's skin which had not been reached by the sun's rays. It is assumed that the persistence of the apparent achromia is due to the continued presence of fungi on the surface of the light-colored patches. When these fungi were destroyed and ultraviolet radiation was administered an increase of pigmentation was noted in the patches.

The nature of the pseudo-achromia was further investigated by the following methods

- 1 Sections of skin from the light-colored areas were removed from two patients and prepared for examination of pigment. Tests made according to the technique of Becker, Praver and Thatcher²¹ showed normal pigment to be present in the basal layer of the epidermis, and chromatophores were also demonstrated in the cutis.

- 2 Scales from lesions of psoriasis, pityriasis rosea and tinea versicolor were collected separately. Equal amounts by weight of the three specimens were then applied to equal areas of skin, and erythema doses of ultraviolet radiation

²¹ Becker, S. W., Praver, L. L., and Thatcher, H. An Improved (Paraffin Section) Method for the Dopa Reaction, *Arch. Dermat. & Syph.* **31** 190 (Feb) 1935.

were administered to these areas. Absolute protection was not obtained in any of the three areas, but there was a noticeable degree of protection in all. The areas covered with scales of *tinea versicolor* showed less erythema and subsequent pigmentation than the areas covered with the other two kinds of scales.

3 Unsuccessful attempts were made to extract fluorescent material from scales appearing on lesions of *tinea versicolor*. The solvents used were alcohol, ether, acetone and physiologic solution of sodium chloride. The scales were allowed to stand in the solvents, being occasionally shaken for over a week. In another unsuccessful attempt, a Soxhlet apparatus was used. It is not known whether the fluorescent material was insoluble in the solvents used or whether the amount of fluorescent material present in the scales was too small to be appreciably noted in the volume of solvent.

4 Fluorescent material from *Microsporon lanosum* and *Trichophyton gypsum* was removed by shaking cultural growths of these organisms with acetone. The solution was allowed to concentrate and applied to test areas of skin and left to dry. An erythema dose of artificial ultraviolet radiation was then administered. A definite screening effect was obtained at the site of application, evidenced by less redness and subsequent pigmentation than in the surrounding skin.

These experiments appear to offer a logical explanation for the pseudo-achromia. The theory of biologic inhibition or destruction of pigment is further discountenanced by analogy when one recalls that thousands of injections of fungous extracts have been administered in the form of injections of trichophytin and that—as far as we know—no pigmentary changes have been reported to have appeared at the site of injection. If *M. furfur* were culturable, this point could quickly be settled. It appears important that *M. furfur* be demonstrated in the scales from the lesion of *tinea versicolor* from which a section is removed for histologic studies of pigment just before material is removed for biopsy. There is no reason why a patient with *tinea versicolor* should not also suffer from vitiligo.

SUMMARY

In fourteen patients with *tinea versicolor*, light-colored patches developed when the affected skin became sunburned. Further exposure to the sun's rays did not result in erythema or in tanning in the light-colored areas, but, on the contrary, they became more prominent owing to an increase in pigment in the surrounding skin. Examination of scales from these areas revealed fungi which were considered to be atypical *M. furfur*. Treatment was carried out for several weeks until no fungi could be demonstrated. Tanning of the skin in the light-colored areas could then be brought about by ultraviolet irradiation. Evidence is offered in favor of the theory that a purely mechanical factor is responsible for the light-colored areas as against the theory of biologic interference with the pigmentary mechanism of the skin. This evidence included (1) an examination for pigment by means of

the dopa reaction, which revealed a normal amount of pigment in the skin, (2) a comparison of scales from lesions of psoriasis, pityriasis rosea and tinea versicolor, which showed that scales from lesions of tinea versicolor protected the skin from ultraviolet rays to a greater degree than scales from lesions of either of the other conditions, and (3) attempts to extract fluorescent material from these scales, which were unsuccessful while, on the other hand, attempts to extract fluorescent material from other fungi in culture proved successful and the extracted material was found to have a screening effect when ultraviolet radiation was administered

The characteristic fluorescence of the lesions of tinea versicolor as seen under filtered ultraviolet rays is of value not only in arriving at a diagnosis but also in determining the extent of the eruption, since lesions not visible in ordinary light can thus be detected. While the lesions of tinea versicolor were usually confined to the trunk, patches were noted in several instances on the back of the neck and on the extensor surfaces of the arms. Failure to treat all involved skin may explain the frequent recurrences noted in this disease.

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SMALL RADIUM NEEDLES IN TREATMENT OF MALIGNANT CUTANEOUS TUMORS

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AND

EVERETT C FOX, M D

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Recent advances in the radiation therapy of cancer have not been fully recognized by American dermatologists, nor have the therapeutic advantages offered by the newer methods of irradiation been widely utilized by them, radiologists, however, have readily adopted these new procedures. Dermatologists have many advantages in their superior ability to diagnose cutaneous lesions and in their more accurate knowledge of cutaneous reactions, and they should adopt these new measures to maintain their therapeutic superiority in the treatment of cutaneous malignant tumors.

Regaud¹ and his associates at the Radium Institute in Paris have proved, both experimentally and clinically, that to obtain the most effective result from irradiation in treating malignant lesions it is necessary to prolong the radiation time. This necessitates diminution of the strength of radium needles when interstitial methods are used or increase of the distance between the source of gamma rays and the area to be treated when surface radiation is employed. More homogeneous irradiation of the mass to be treated may be obtained by the use of multiple, equally spaced points of radiant energy.

Régaud obtained sterilization of a ram's testis by prolonged irradiation with feeble doses of gamma rays, although he failed to do so by using five times the dose for a shorter period. From this experiment he concluded that the cells were more radioresistant at certain stages of their life cycle than at others. He stated "In the center of the ram's testicle, 15 dose units of heavily filtered emanations, acting during a few hours only, produced a central necrosis without sterilizing the outer parts of the organ, in remarkable contrast, 3 dose units acting during 15 days, have effected complete sterilization, but without necrosis." The application of this observation to the treatment of

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Read at the Fifty-Ninth Annual Meeting of the American Dermatological Association, Inc, Swampscott, Mass, June 6, 1936

¹ Regaud, C. Some Biologic Aspects of the Radiation Therapy of Cancer, *Am J Roentgenol* 12 97 (Aug) 1924, Radium Therapy of Cancer at the Radium Institute of Paris, *ibid* 21 1 (Jan) 1929

cancer has given greatly improved results, and some types of squamous cell carcinoma which were previously considered as radioresistant have proved to be radiosensitive. The radiation treatment of cancer should utilize this selective action of the rays instead of their diffuse caustic effect.

These new principles were first used by Régaud, who employed multiple radium tubes at increased distance. This biologic principle was then adapted to interstitial therapy by Cade.² The work was further developed by Evans and Cade and by Birkett, British radiotherapeutists, in this country it was carried out by Kaplan,³ Lenz,⁴ Martin,⁵ Soiland,⁶ Treves,⁷ Cole and Driver⁸ and others. Similar biologic principles have been utilized by Coutard⁹ in his plan for a multiple dose of heavily filtered roentgen radiation, and J M Martin and C L Martin¹⁰ have described a modification of Coutard's technic. With the addition of filtration, these methods are but revivals of the broken dose method of roentgen irradiation advocated by Pusey¹¹ more than thirty years ago.

In this communication we propose to deal with the technic and dosage in the use of platinum iridium needles containing small amounts

2 Cade, S (a) Radium Therapy of Cancer of the Buccal Cavity, *Lancet* 1.8 (Jan 5) 1929, (b) Radium Therapy of Cancer, New York, William Wood & Company, 1929

3 Kaplan, I Radium Treatment of Cancer of the Breast, *Am J Roentgenol* 25:250 (Feb) 1931

4 Lenz, M Curie Therapy of Epidermoid Carcinoma of the Intra-Oral Group as Carried Out at the Institute of Paris, *Am J Roentgenol* 15:216 (March) 1926, Radium Therapy of Cancer, *Arch Phys Therapy* 14:393 (July) 1933

5 Martin, C L Small Radium Needles Versus Radon Implants, *Am J Roentgenol* 27:240 (Feb) 1932

6 Soiland, A Diagnosis and Treatment of Carcinoma of the Breast, *Southwestern Med* 17:153 (May) 1933

7 Treves, N A Small Platinum Needle Designed for the Use of Various Strengths of Radium Element Interstitially, *Am J Roentgenol* 33:537 (April) 1935

8 Cole, H N, and Driver, J R Radium Dosage and Technic in Carcinoma of the Skin, *Am J Roentgenol* 33:682 (May) 1935

9 Coutard, H Roentgen Therapy of Epitheliomas of the Tonsillar Region, Hypopharynx and Larynx from 1920 to 1926, *Am J Roentgenol* 27:313 (Sept) 1932

10 Martin, J M, and Martin, C L Modified "Coutard" Roentgen Therapy, *J A M A* 104:605 (Feb 23) 1935

11 Pusey, William Allen Roentgen Rays in the Treatment of Skin Diseases, *J A M A* 37:820 (Sept 28) 1901, Report of Cases Treated with Roentgen Rays, *ibid* 38:911 (April 12) 1902, A Subsequent Report on a Case of Carcinoma Discharged as Hopeless and Recorded as a Failure, *ibid* 39:487 (Aug 30) 1902, The Rationale and the Indications for the Therapeutic Use of Roentgen Rays, *J Cutan Dis* 29:355 (Aug) 1903, Therapeutic Use of X-Rays Three Years After, *J A M A* 44:1496 (May 13) 1905

of radium for prolonged interstitial irradiation in selected cases of cutaneous malignant disease

The object of all radiation therapy is to administer a lethal dose to each cell of the neoplasm. To obtain satisfactory clinical results it is necessary to administer a homogeneous dose sufficient to produce disintegration of the tumor with the least possible damage to the healthy surrounding tissues. We believe that this is best accomplished by means of the small platinum needle with multiple interstitial focal points of radiation.

DESCRIPTION OF NEEDLES

The platinum iridium needles used by us are of the French-British type and contain 1 and 2 mg of radium element. Our needles contain slightly more radium element than the original needles described by Cade,^{2a} which reduces the length of time the needles must remain in the tissue without altering the original purpose of prolonged irradiation.

Our small needles are 11 mm long and 1.5 mm in diameter, contain 1 mg of radium element and have a wall thickness of 0.5 mm of platinum. The larger needles are 27 mm long and 1.85 mm in diameter, contain 2 mg of radium element and have a wall thickness of 0.6 mm of platinum. This gives 1 mg of radium element to each centimeter of active length of needle and when needles are implanted at 1 cm distance gives proper distribution of homogeneous gamma rays to 1 cc of tissue.

DOSAGE

It has previously been estimated that with needles of this type 100 milligram hours of irradiation per cubic centimeter of tissue will destroy squamous cell carcinoma without causing necrosis or sloughing. Therefore, our needles were at first allowed to remain in place for 100 hours, or four and one-sixth days. The time element has gradually been increased until at present they are allowed to remain in place for five or six full days, which gives from 120 to 140 milligram hours of irradiation. Recently one of us (B. S.) has prolonged the time to seven full days in the treatment of extensive clinically resistant lesions, producing 168 milligram hours for each needle. The erythema was only moderately increased and the epithelitis only slightly more marked, no evidence of sloughing or necrosis was observed. A dose this large has been used by Treves⁷ and by Cole and Driver⁸ in treating cutaneous malignant tumors with excellent results. The large dose apparently does not delay healing, which is usually complete in from three to eight weeks, depending on the size of the tumor treated. In marked contrast to the former method of interstitial irradiation with insufficiently filtered steel needles and subsequent necrosis due to beta

rays, the present method of prolonged irradiation with heavily filtered platinum needles is accompanied by little or no pain. Local pruritus is usually the most marked subjective symptom.

TECHNIC OF NEEDLE IMPLANTATION

The needles are implanted 1 cm apart underneath and at the margins of the neoplasm, the usual surgical asepsis with local or block anesthesia being employed. We do not implant our needles directly into the tumor itself but always place them at the extending borders of the neoplasm, where irradiation is theoretically most needed. For the introduction of the needles a fine-pointed scalpel is used for making

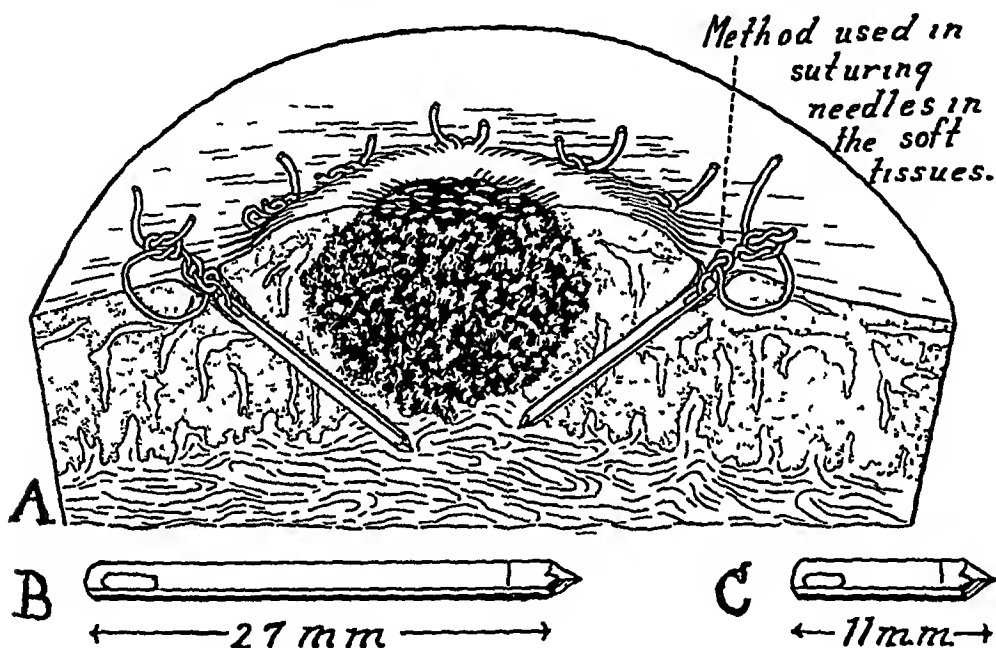


Fig 1—Schematic drawing showing types of needles employed and the method of implantation. *A*, surface and sagittal views of cutaneous malignant tumor with needles sutured in place, one needle to each cubic centimeter of tissue. The needles were allowed to remain in place for one hundred hours, producing 100 milligram hours per cubic centimeter. *B*, large needle, the dimensions of which are as follows: length, 27 mm; diameter, 1.85 mm; wall thickness, 0.6 mm. The wall is platinum, the needle contains 2 mg of radium. *C*, small needle 11 mm long and 1.5 mm in diameter, having a wall thickness of 0.5 mm and containing 1 mg of radium.

a puncture wound, which facilitates the insertion of the needles. The eyelet of the needle is threaded with heavily waxed dental floss and tied so that there are a short, 2 inch, and a longer, 6 or 8 inch, suture. After the needles are inserted a small full-curved needle is threaded to the short suture, a transfixion suture is placed through the puncture wound and a tie is made with the two ends of dental floss suture. The longer, or guy, end is then attached to an adjacent area with adhesive tape. If one prefers, dermal suture may be threaded through the eyelet

of the radium needle and used for the transfixion suture, the dental floss being used only as a guy thread. In either case the needles are removed by clipping the transfixion suture and applying gentle traction to the dental floss.

INDICATIONS, ADVANTAGES AND RESULTS

The choice of cases of cutaneous malignant disease in which this method of implantation therapy should be used is governed by many factors. The method is especially valuable in treating extensive malignant lesions which are difficult to treat by any other technic, and it gives results superior to those obtained by any other method in the treatment of lesions which are situated adjacent to, or have produced infiltration of, bone or cartilage. Resistant lesions in any location, especially those which have failed to respond to other methods, and lesions with extensive formation of scar tissue are more amenable to this type of implantation therapy than to other methods. In general,



Fig 2—Pedunculated basosquamous cell carcinoma of the lower eyelid. The eyeball was not involved. Two needles containing 2 mg. of radium were implanted at the base of the growth for one hundred and twenty hours (five days). The total dose was 480 milligram hours. The second photograph was made one year later.

the technic is advantageous in cases of rapidly growing squamous cell carcinoma of any site, of extensive and infiltrative basal cell carcinoma and of a neoplasm overlying or involving bone or cartilage.

The primary advantages of implantation therapy over radium therapy externally applied are the homogeneous irradiation of the entire area of malignant degeneration and the continuous treatment over a prolonged period, with the resultant irradiation of the tumor cells during periods of mitotic division, when they are most radiosensitive. The prolonged continuous treatment prevents the development of radio-resistance. The delayed time of healing which may follow the use of radon seeds or heavy doses of surface irradiation is avoided. The objectionable radiation inflammation of bone and cartilage is prevented, more accurate dosage is possible and the technic may be more safely applied to large areas without the danger of cutaneous sequelae such as result from surface irradiation. The greatest disadvantage is the necessity of hospitalization in many cases. When lesions of the skin

are irradiated with the needles well sutured and fixed dressings are applied, patients need not be hospitalized. In the treatment of malignant disease affecting movable areas, as the lip or the oral cavity, hospitalization is often required.



Fig 3—Large basal cell epithelioma infiltrating deeply into the tissues of the cheek. Six needles containing 2 mg and three needles containing 1 mg of radium were implanted underneath and at the margins of the growth for one hundred and twenty hours (five days). The total dose was 1,800 milligram hours. The second photograph was made one year later. There was no recurrence, and an excellent cosmetic result was obtained.

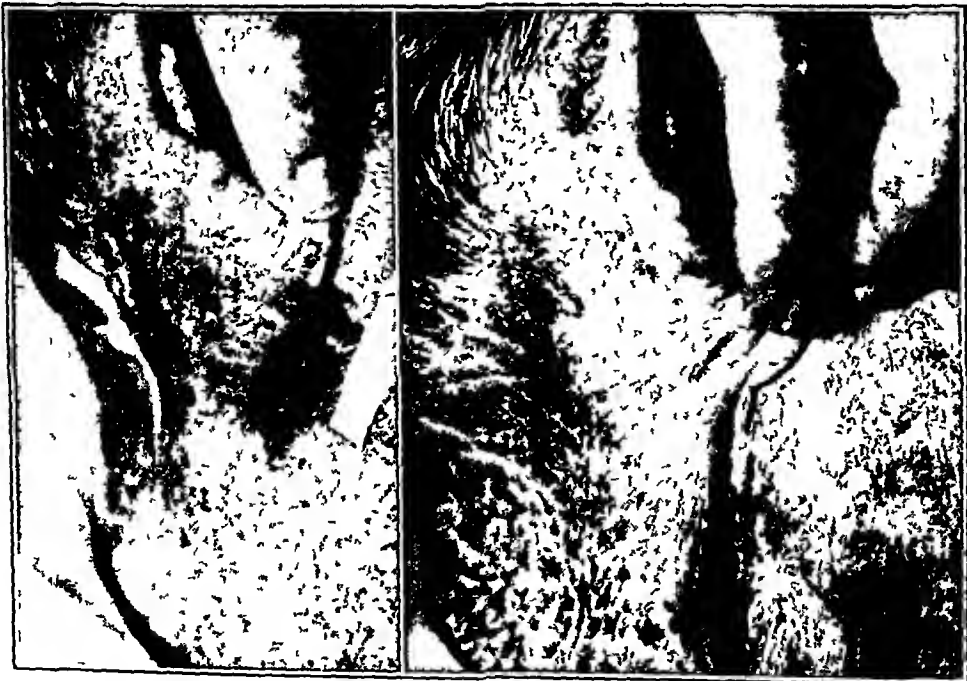


Fig 4—Large, rapidly growing prickle cell carcinoma. Six needles containing 2 mg of radium were implanted beneath and at the margins of the lesion for one hundred and forty-four hours (six days). The total dose was 1,728 milligram hours. The second photograph, made seven weeks after insertion of the needles, shows complete healing.



Fig 5—Prickle cell carcinoma of the index finger with attachment to underlying structures. Three needles containing 2 mg of radium were implanted at the base of the growth for one hundred and twenty hours (five days). The total dose was 720 milligram hours. The second photograph was made eleven months later.



Fig 6—Prickle cell carcinoma infiltrating deeply into the subcutaneous tissues of the lip. Three needles containing 1 mg of radium were implanted at the margins of the infiltrated area for one hundred and twenty hours (five days). The total dose was 360 milligram hours. The second photograph was made seven months later.



Fig 7—Recurrent prickle cell carcinoma in scar tissue at a site previously treated by a "cancer-paste." Two needles containing 2 mg of radium were implanted at the margins of the growth for one hundred and twenty hours (five days). The total dose was 480 milligram hours. The second photograph was made one year later.

The results in our cases have been satisfactory, and cures have been attained which might not have been achieved by any other method. Recurrences following surgical treatment, desiccation or previous irradiation have responded rapidly. Our series of sixty-six neoplasms



Fig 8—Prickle cell carcinoma of four months' duration. Three needles containing 2 mg of radium were inserted at the base of the lesion for one hundred and nineteen hours. The total dose was 714 milligram hours. The second photograph was made three months later.

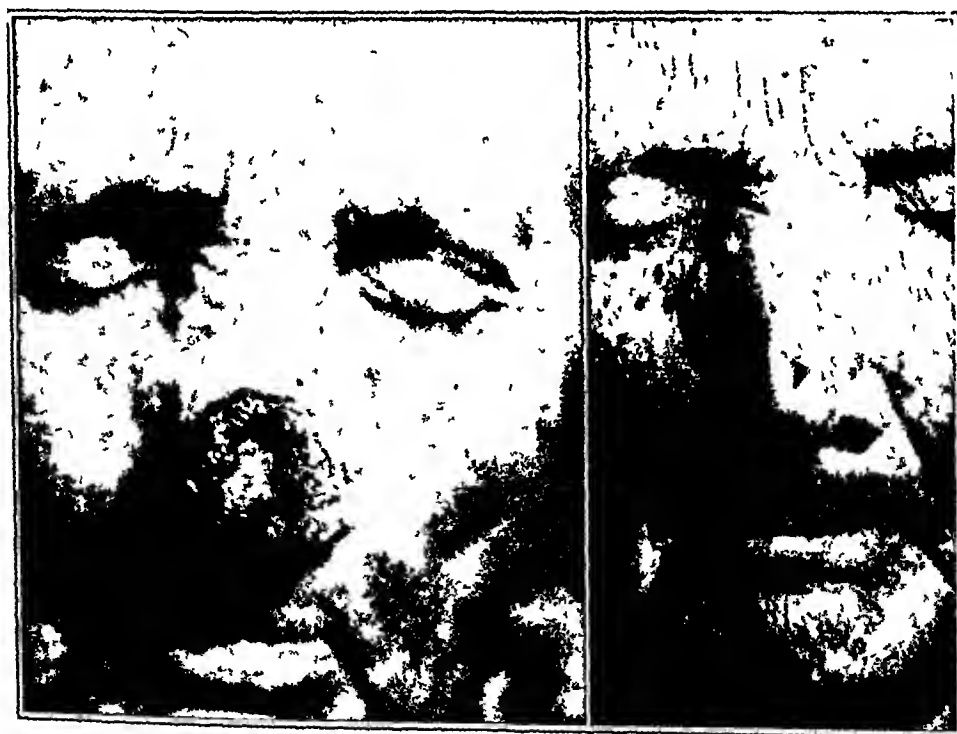


Fig 9—Prickle cell epithelioma of the nose. The lesion had received an unknown quantity (twelve treatments) of roentgen radiation one year previously. Nine needles containing 1 mg of radium were implanted at the base of the growth for one hundred and ten hours. The total dose was 990 milligram hours. The second photograph was made four months later.

treated by this method includes lesions of the lip, nose, face, scalp, dorsum of the hand, side of the neck and other sites of skin and mucous membrane. Treatment in selected cases of intra-oral carcinoma by this technic has resulted in local cure, yet the percentage of metastatic lesions has apparently not been materially decreased.

SUMMARY

A method of radium implantation therapy in which the dose can be carefully and accurately measured is presented for use in treating cutaneous malignant disease.

Prolonged interstitial irradiation with heavily filtered platinum-iridium needles of small radium intensity produces a homogeneous irradiation with selective gamma rays.

Photographs showing the lesion before and after treatment with a given dose of radiation are presented. Excellent cosmetic results are obtained, since protection is afforded the surrounding normal tissues because of the heavy filtration and the multiplicity of foci.

The method has been used by us for more than three years, it is continually becoming more useful, and its advantages are more readily recognized. It is recommended for use in selected cases of cutaneous malignant disease and not as a routine procedure for the treatment of surface and intra-oral neoplasms.

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ABSTRACT OF DISCUSSION

DR C FERD LEHMANN, San Antonio. The application of this principle of radiation, i. e., application of heavily filtered rays in small doses over a continuous period, has two advantages: not only does it reach, and effect cures on, the so-called radioresistant cells but it also leaves a much healthier scar. I have noticed in the past few years that lesions so treated, particularly those on the lips, leave scars much more healthy than do lesions treated with monometal needles. This procedure has many advantages in treatment of epithelioma around cartilage in the nose and ear in cases in which reconstructive surgical measures will become necessary. However, this method of treatment is used in many cases of epithelioma in which other methods, such as curetting and electrodesiccation, could be employed. I think that eventually Dr. Shelmire's enthusiasm will wane and he will use the method only in carefully selected cases.

DR HAROLD N. COLE, Cleveland. My co-workers and I have used these radium-platinum needles since shortly after Cade's text book (*Radium Treatment of Cancer*, New York, William Wood & Company, 1929) was published. Any dermatologist who is interested should read that book and review the type of treatment with gamma rays described in it. The method should not be used as a routine. I think that in many cases excellent results can be obtained with endothermy and curettage. On the other hand, there are many cases in which platinum needles containing radium are of great value. In cases of carcinoma of the lip certain types of lesions of the mucous membrane will respond better to this treatment than to any other.

The original treatment for carcinoma of the tongue was surgical intervention, and it is known that disastrous results followed that type of treatment. When radium began to be used it was first employed in the form of plaque application. Later the scheme was devised of using steel needles. This was not quite satisfactory. Still later Quick introduced the use of glass seeds. The reaction from glass seeds was tremendous, but several patients who were cured by the use of glass seeds exhibit extensive disfigurement. Then gold seeds were devised. The reaction from these was not so severe, nevertheless, it was considerable. Platinum radium needles and gamma rays provide the ideal treatment for carcinoma of the tongue. With the area under local anesthesia the needles are placed in position and sewed in, and string previously soaked in a 5 per cent solution of acriflavine hydrochloride to prevent digestion is attached to the individual needle and then brought outside the mouth and attached with adhesive tape to the cheek. It is remarkable how little discomfort these needles cause, within twenty-four hours after they are inserted the patient is able to eat tolerably well. When they are removed there is a reaction that appears in about ten days and lasts for from four to six weeks. The results are good in a fair proportion of cases, naturally not in all.

The needles are of great value in treatment of recurrence after radiation therapy. A patient may have received roentgen therapy, and the tumor may be bound down to the bone, making surgical treatment undesirable. In a case of that type platinum needles will produce surprisingly good results. One must be careful not to give too much radiation, for the tissue has lost much of its blood supply, and if too much radiation is used healing will be slow.

The scar left after this therapy is soft, supple and inconspicuous. The method is also of great value in treating lesions on the ear, which in the past have proved troublesome and in many cases have produced metastases. The same thing is true of lesions about the nose.

I think that dermatologists should use this method of therapy more often.

DR HOWARD MORROW, San Francisco. Notwithstanding the fact that we treat epithelioma of the lip with electrodesiccation, my co-workers and I are still believers in radium therapy.

Dr Cole referred to the treatment of lesions of the mucous membrane with radium, and I agree that it is the best method known. Dr Taussig has long ago adopted the use of gold seeds, and the reaction which for many years followed the use of glass seeds does not result from treatment with gold seeds.

As to selection of cases, I am sure that eventually Dr Shelmire will stop using radiation in treating carcinoma of the ear. One of these days he will have an experience which will make him believe in destruction of lesions of the ear by electrodesiccation and not by radium therapy.

It does not matter, as has been said, what type of treatment is used provided it is thorough. I think that fewer recurrences will follow desiccation than have followed radium therapy.

DR GEORGE MILLER MACKEE, New York. I wish to call attention to one point that has been a subject of controversy in the past but about which less is heard nowadays, namely, the danger of inserting anything in a malignant tumor—a knife, a punch, a radium needle or an implant. Years ago it was thought that this was a dangerous procedure because it led to metastasis. I have discussed this subject with almost every one of the well known cancer experts of the country and with many pathologists—Dr Ewing, Dr Francis Carter Wood, Dr Douglas Quick and many others. I find now that the consensus is that there is no danger at all in

such a procedure These experts say that there is danger if the lesion is squeezed unnecessarily or massaged but that the introduction of a sharp punch or needle is without danger

The radium needle is a valuable method and should be, I think, used in selected cases I think there are some cases in which it is better to use beta rays I do not have time to go into details, but in cases of epithelioma of the eyelids, for example, I prefer to use needles or implants that will give intense beta rays In that way there is much less danger to the eye

I may have misunderstood Dr Shelmire, but I thought he said that one could depend on obtaining cure in 95 per cent of unselected cases That has not been my experience I think that the highest incidence of cure that one can hope to obtain by any method in unselected cases is about 85 per cent In selected cases of basal cell epithelioma of pure type and by the use of a selected method one can expect an incidence of cure of between 95 and 100 per cent on the basis of the five year period of observation I believe that every dermatologist should be expert in all the accepted methods of diagnosing, determining radiosensitivity of tumors and grading and managing cutaneous malignant degeneration

DR LAURENCE R TAUSSIG, San Francisco The radiation therapy of malignant disease has been developing for thirty years and is still in flux I think that ideas regarding radiation therapy change from year to year, partly because of what is learned about that form of therapy and partly on account of the development of other types of apparatus The interstitial method was one of the earliest methods devised, and it has been greatly improved At first radon contained in glass seeds was used, and I think that in some cases the glass seeds would give results superior to those obtained with gold seeds or with the new platinum needles My co-workers and I still use irradiation in a number of cases of malignant degeneration In some cases we use roentgen therapy I think that some lesions, particularly those of the back of the hands, respond well to unfiltered roentgen radiation

I do not agree with Dr Shelmire that the implantation of seeds in involved lymph nodes is always hopeless In a few instances my co-workers and I have implanted gold seeds in rather large lesions which the surgeon did not wish to remove, and within a few months the glands have become movable and fit for surgical removal In a few instances long time cures have resulted

DR BEDFORD SHELMAIRE We use this method of irradiation only in selected cases Most of the epitheliomas seen in dermatologic practice can be treated effectively by Sherwell's method, electrothermic coagulation, cautery removal or even excision with the scalpel, all destructive methods should be followed by some form of irradiation We employ all these methods in our practice

We prefer these heavily filtered needles to gold seeds because of the lower expense, heavier filtration, ease of introduction and more homogeneous irradiation After the initial purchase the needles are always available After irradiation of the growth they are removed and are not left in the tissues as foreign bodies, as is the case with the seeds

I agree with Dr Morrow that most epitheliomas of the ear are readily curable by methods other than irradiation with these small needles In certain selected cases these needles seem superior to any other form of treatment

Dr MacKee is certainly correct in advocating treatment with beta rays in most cases of epithelioma of the eyelids As to the percentage of cures in cases of cancer of the skin, I still believe that I can effect a cure in more than 95 per cent of cases observed in private practice

VITILIGO OF THE LIPS

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SAN FRANCISCO

Vitiligo, except for the disfigurement it causes, is an uninteresting disease, as it is easily diagnosed, is an indication of no other known trouble and is in most instances absolutely refractory to treatment. It is manifested merely by an area of white skin surrounded by more deeply pigmented skin, as if the pigment had been shoved from this white center to the periphery. Formerly the condition was more interesting than it is at present, as it was thought to be a symptom of leprosy and the patient exhibiting it was expelled from his community, which was then equivalent to a death sentence, but that time has long passed.

The statement that the area of vitiligo is white is not exact. It is white only by contrast. If a hole is cut in a piece of white paper and placed over the apparently white surface, thereby shutting out the surrounding, more deeply pigmented, skin, it will be found that the surface is not white but pink. This has a bearing on what is about to be related.

A Japanese farmer aged 39 consulted me in March 1936 because of scaly roughness of the lower lip. The upper lip was also affected but not nearly so extensively. There were numerous patches of vitiligo scattered over the body and limbs about which the patient was worried and for which he had received treatment by cauterization from a Japanese physician.

In examining the lips my interest was of course fixed on the superficial lesions, but I felt that there was something strange and unusual in the basic tint until it dawned on me that the lips as well as the skin were vitiliginous. Instead of being a deep red or even dark, as would be natural in a Japanese, the exposed portion was light salmon pink except in limited areas of the upper lip and also to a lesser extent of the lower lip, where it was deep brown. This was quite in accord with the picture of vitiligo in which the neighboring skin, as stated, always exhibits an excess of pigment.

The appearance may easily cause one to fall into error, as pigmented patches, especially on the exposed red portion of the lower lip, are not uncommon and, as Pusey long ago mentioned, are not necessarily serious. The pigmented areas exhibited by this patient, however, when once appreciated, appeared as something strange and unnatural, and the statement that the depigmented surfaces were salmon pink conveys lamely the impression they made.

Mention of such an occurrence as this is rare in the literature Brunauer¹ and Coulon-Esquier stated that vitiligo of the mouth occurs only in Negroes, and Atkinson mentioned vitiligo of the labia minora and of the inner surface of the prepuce In Pusey's textbook² there is an illustration showing vitiligo of the eyelids and of the lower lip in a dark-skinned person



Photograph showing a characteristic white area over the right temple with the usual hyperpigmented skin about it, the more highly pigmented mucous membrane above the vitiliginous upper lip and the hyperpigmented area to the right on the lower lip The latter is slightly blurred because of the scaling The white areas at the corners of the mouth are characteristic and do not occur in leukoplakia

The unusual situation was, however, not the only or even the chief interest in this case It is repeatedly mentioned in the literature that

1 Brunauer, Stefan Robert Atrophien, in Arzt, L, and Zieler, Karl Die Haut- und Geschlechtskrankheiten, Berlin, Urban & Schwarzenberg, 1935, p 779

2 Pusey, William Allen The Principles and Practice of Dermatology, New York, D Appleton & Co, 1917, p 962 The illustration is from Heidingsfeld's collection

the pigmented areas of vitiligo are unusually sensitive to actinic solar rays. The patient's home was near Stockton, Calif., which is at 37° 50' degrees north latitude, the latitude of the southern part of Spain, he was therefore exposed to strong rays of the sun, though they were of about the same strength as those prevailing in his native country.³ Confirmatory evidence of the effect of this irritation was shown by the fact that the lower lip was much rougher and more irritated than the upper. This continuous irritation in such a situation is a serious matter, as it leads to cancer.

As nothing could be done to repigment the lips and as the man's occupation was fixed, the therapy was naturally directed toward shielding the lips from actinic rays. Red is the best color for this. The principle of using a red shield is the same as that which is employed by photographers in changing photographic plates under a red light. This principle induced the farmer in the old days to use a red bandana to screen the back of his neck and the cowboy to use one to screen his face, with the difference that the farmer tied the knot in front and the cowboy tied the knot behind. In both instances the use of the bandana was a subconscious defense reaction. It may be possible for the cowboy to wear a red bandana over the face, but it is, however, impossible for a farmer to do so as the practice would interfere with his work.

The use of another kind of screen was suggested, one of the large umbrella-like hat so frequently seen in Japan, but never worn by Japanese in this country, probably because the Japanese, being highly sensitive, are averse to being made conspicuous by wearing such a hat.

Another screen is the common lip-stick, which is adherent and, if not perfumed, is usually nonirritating.⁴ The patient therefore was advised to wear a broad-brimmed hat, to use a lip-stick during the day and to apply a mild adherent ointment at night.

By far the best screen, however, is the natural one provided by the moustache, and the dark color of the patient's moustache area, as seen in the photograph, was principally due not to the hyperpigmentation of vitiligo but to stout black hairs holding out a promise that if they were allowed to grow an excellent black screen would be formed. Why nature in the tropics and subtropics has chosen black, an absorbing color for radiant energy, as her favorite screening color for human beings while in the northwestern part of Europe, where the sun is weak, she has chosen red and yellow is one of her mysteries.

This was not my first experience with the moustache as an efficient screen. I had advised that natural protection in the treatment of solar

³ Tokyo, Japan, is a little north of 36 degrees latitude.

⁴ Baer, Harry Leonard. Lip-Stick Dermatitis, *Arch. Dermat. & Syph.* 32:726 (Nov.) 1935.

irritability of the lower lip in 1911, in a case in which I became aware of the inefficiency as a screen for the lips of the red bandana for a man working on a farm

Not much can be said in praise of the hairy covering of man. It is expensive to wear or to get rid of, and it harbors dirt, microbes and vermin and favors disease. As a coat it is ridiculously thin and ragged and has been superseded by clothing. It is cheering, however, to find, as in this case, that it has some use.

PROBABLE CASE OF THIRD GENERATION SYPHILIS

REPORT OF A CASE

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Although third generation syphilis is exceedingly rare, there is sufficient evidence in the literature to show that it does occur. There are, however, a number of syphilologists of long experience who are skeptical of its occurrence. They have stated the belief that the majority of cases reported do not fulfil all the criteria first proposed by Fournier and Finger Stokes,¹ who expressed the belief that most of the cases that have appeared in the literature were not beyond criticism, quoted these criteria as follows

"(1) Acquired syphilis must be demonstrated in the grandmother and preferably also the grandfather (2) Prenatal as distinguished from acquired syphilis must be demonstrated in the mother of the third generation case. Acquired syphilis must be excluded in her case and the father must be proved to be healthy (3) There must be incontestable evidence of prenatal syphilis in the third generation, and (4) manifestations must appear soon after birth in both the second and third generation "

Rosenbaum and Faulkner² recently reported two complete family histories which they believe fulfil all the criteria for proving the occurrence of syphilis in the third generation. Smith and Howard, of Moore's clinic,³ made a study of this condition and found that eighty-eight mothers with congenital syphilis had one hundred and seventy-one children, of which eight (4.5 per cent) had third generation syphilis.

The following complete case history is reported because we believe that it essentially fulfils the criteria proposed by Fournier and Finger

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University, Dr George M MacKee, Director, service of Dr Fred Wise, and the New York Infirmary for Women and Children, Department of Obstetrics, Dr W A Ragland, Director

1 Stokes, J H. *Modern Clinical Syphilology*, Philadelphia, W B Saunders Company, 1934, p 1270

2 Rosenbaum, H A, and Faulkner, H L. *Third Generation Syphilis*, J Pediat 7 735, 1935

3 Moore, J E. *The Modern Treatment of Syphilis*, Springfield, Ill, Charles C Thomas, Publisher, 1934, p 442

REPORT OF CASE

The grandmother, aged 54, an Italian, first reported to her physician in 1920, complaining of nervousness. Her physician made a test of the blood and then gave her ten injections in the arm and the hip. She consulted one of us (F S) in November 1935, complaining of dizziness, noises in the right side of the head, diarrhea, restless sleeping, drowsiness, frequency of urination and nocturia. A test of the blood at this time was positive for syphilis. Her husband died at the age of 32, after an automobile accident. He had contracted a chancre many years previously and reported to his private physician for treatment. The physician did not remember the exact date on which the patient was first seen but thought that it was about twenty-four years previously. The patient received three injections but did not return for further treatment. From this union, which was not consanguineous, there were eight pregnancies. Six siblings were living and came under our observation. The status of each one as far as syphilis is concerned is given in chronological order according to the mother's pregnancy.

First Pregnancy—Mrs Fo was born in 1907 and married Mr Fo in 1931, they had no clinical or serologic evidence of syphilis.

Second Pregnancy—Mrs Fi was born in 1910 and married Mr Fi in 1930, they had no clinical or serologic evidence of syphilis. They had one child, who was born in 1931 and who was also free from evidence of syphilis.

Third Pregnancy—C C was born in 1911, contracted whooping cough and died of convulsions at the age of 19 months. No evidence in the history suggested a syphilitic stigma.

Fourth Pregnancy—Mrs L was born in 1912, at birth she presented no stigma of congenital syphilis as far as could be elicited from the history. Routine tests of the blood were made in 1935, when it was learned that her mother had syphilis. Mrs L showed a 4 plus reaction to the Kline, Wassermann and Kahn tests of the blood. She married Mr L in 1931, he had numerous serologic tests, all of which gave negative results. They had one child, born in 1932, who presented no stigma of congenital syphilis. The Wassermann, Kline and Kahn tests of the blood, however, were strongly positive on numerous examinations. Mr L's mother was also examined, she had no clinical or serologic evidence of syphilis.

Fifth Pregnancy—The child, born in 1913, had a cold and snuffles from date of birth and "wasted away until she died, at the age of 4 months."

Sixth Pregnancy—D C was born in 1915 and presented no stigma of congenital syphilis. The Wassermann, Kline and Kahn tests of the blood, however, elicited a strongly positive response on numerous examinations. He gave no history of having had a primary lesion or secondary eruption.

Seventh Pregnancy—R C, born in 1919, never presented any stigmas of congenital syphilis. Routine serologic tests performed in January 1936 gave the following results: Kline test, 2 plus, Kahn test, negative, Wassermann test, negative.

Eighth Pregnancy—L C was born in 1921. He never presented any stigma of congenital syphilis, and the Wassermann, Kline and Kahn tests of the blood gave negative results on numerous examinations.

It is interesting that the mother had received intramuscular and intravenous injections immediately preceding and during the last pregnancy.

Roentgenograms of the long bones and of the skull of Mrs L , her child and her brother (D C) disclosed no changes due to syphilis

COMMENT

Acquired syphilis was demonstrated in both the maternal grandmother and the maternal grandfather. It is impossible, however, definitely to prove the occurrence of congenital syphilis in the mother of the patient with third generation syphilis, especially since she presented no stigma of congenital syphilis. Nevertheless, several facts strongly suggest this possibility

1 The grandfather acquired his infection about twenty-four years previously, i e , immediately before the birth of the mother of the patient with third generation syphilis

2 The two older sisters were nonsyphilitic, while serologic tests of the younger brother were positive for syphilis

3 The mother of the patient with third generation syphilis gave no history of having had a primary lesion or a secondary eruption during her early adult life. In addition, her husband had no clinical or serologic evidence of syphilis

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LXXV—MYCOLOGIC TECHNIC IN DERMATOLOGIC PRACTICE

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In every case of suspected mycosis the causative organism should be isolated and studied whenever practicable because from the academic standpoint the possibility of the presence of a new or different pathogen should not be overlooked

The methods herein described are intended for use in routine office work

SCRAPINGS, METHODS AND MATERIALS

The most common method used for the examination of scrapings is to mount the material in an alkali, either sodium hydroxide (NaOH) or potassium hydroxide (KOH) may be used Potassium hydroxide is preferable, it should be used in a 10 to 30 per cent solution For rapid work, a 40 per cent solution may be used, but it is not advocated Too weak a solution takes a long time in clearing the skin, whereas too strong a one tends to swell and disintegrate the fungi The length of time necessary for the clearing varies from five minutes to approximately two hours A little heat often facilitates the procedure It is not necessary to allow the material to stand overnight Care should be taken when examining the slide (1) to ring it with paraffin to prevent evaporation and consequent crystallization and (2) to use subdued light in order to avoid high lights The fungus appears distinct and is clearly discernible as contrasted with the irregular and nondescript appearance of the skin, which usually becomes clear

The type of material to be examined varies with the several infections, and different methods of study should be applied to the scrapings Of diagnostic importance, however, is the type of mycelium seen in the mounts, whether fragmented or continuous, simple or branched The distribution of the spores and their size facilitate diagnosis

In scraping lesions care should be taken to obtain portions from the active infection, particularly the border In vesicular eruptions the

Submitted for publication, Feb 13, 1936

From the Laboratory for Mycological and Dermatological Research of the Research Department of the Barnard Free Skin and Cancer Hospital

Studies, observations and reports from the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, Department of Dermatology, service of Drs M F Engman and W H Mook

fluid does not often contain the fungus except possibly in yeastlike infections. In eruptions caused by filamentous fungi the roofs of the vesicles should be examined and cultured. The lesion should always be cleansed with 70 per cent alcohol before the material is removed. This concentration is preferable to 95 per cent because of its greater ability to destroy the surface contaminants. In the case of ulcerated and crusted vesicular or papular lesions care should be taken that fresh infections are scraped to obtain active organisms.

The hydroxide method of examination is simple and often rapid, but unless it is used by one accustomed to its mode of action the results may be misleading. The observations may be confused with the presence in the mounts of structures which resemble fungi closely, such as crystals, the so-called "mosaic fungus" and distorted globules of fat. Consequently a number of methods using stains or dyes have replaced those using an alkali with marked success.

When the scales or scrapings are rather thick the stains are not used to great advantage, and recourse must often be had to potassium hydroxide. When the material is fairly thin, however, such as is the case in examination of dandruff scales for *Pityrosporum ovale*, of scrapings from pityriasis versicolor, of dermatomycoses of the ring-worm type or even of pus, exudates and sputum, a 1 per cent aqueous solution of methylene blue and glycerin can be used as follows. One drop of the 1 per cent solution of methylene blue is placed on a clean slide, and the material is stirred within it. The scrapings should be thoroughly immersed in the stain. This is allowed to stand for approximately two minutes, then a clean cover slip is placed over the mixture and pressed down to flatten out the material and to express the excess solution. The superfluous stain is taken up by filter paper. A drop of glycerin is then placed along one edge of the cover slip and allowed to seep under, displacing the stain and giving a clear background to the stained material. The fungus appears bright blue.

Another method, which is similar, substitutes an undiluted Giemsa solution for the methylene blue. The Giemsa solution is made up with glycerin, and distilled water is placed along the edge of the cover slip in place of the glycerin used in the aforementioned method. This procedure has been followed with good results by Weidman. These preparations, however, are temporary, but they are of value in that they bring out detail and prevent shrinkage and distortion of the cells.

The value of cotton blue (aniline blue, China blue) and lactophenol mounts of tissue or material has never been strongly emphasized. It has been used almost exclusively for culture material and has been employed only occasionally for scrapings. The dye is made up as a 0.5 per cent aqueous solution. The lactophenol is made up as follows

lactic acid (U S P), 20 Gm, phenol crystals, 20 Gm, glycerin, 40 Gm, and distilled water, 20 Gm. A drop of the cotton blue is placed on the slide, the material is stirred up within it and allowed to stand for approximately two minutes. The cover slip is added and pressed down to squeeze out any excess dye, which is then taken up by filter paper. A drop of lactophenol is added to the edge of the cover slip and allowed to replace the cotton blue which dries out. The stain may be rapidly replaced by holding a bit of filter paper at the edge of the cover slip opposite the drop of lactophenol. This stain and the clearing agent (lactophenol) are useful in that the cell wall stains lightly as compared with the darkly colored central portion.

Swartz recently made the following modification in the lactophenol and cotton blue procedure. The scrapings are first placed in a 5 per cent solution of potassium hydroxide, heated somewhat and then washed in water. The material is then put into a drop of the combined cotton blue (0.5 per cent) and lactophenol. If the technic is successfully carried out, the fungi stain blue against a background which has been cleared by both the potassium hydroxide and the lactophenol. This procedure should be followed with care since the alkali (KOH) has a tendency to hinder the taking up of stain. The combined cotton blue and lactophenol tend to give a blue background and should therefore be used separately, as described.

A solution stronger than lactophenol for clearing is obtained by using the following ingredients: phenol crystals, 25 Gm, lactic acid (U S P), 25 Gm, and chloral hydrate crystals, 50 Gm. For thick material the following combination is recommended by Langeron: chloral hydrate crystals, 40 Gm, phenol crystals, 40 Gm, lactic acid (U S P), 20 Gm, and sodium salicylate, 10 Gm. A little heat facilitates clearing.

The investigation of infections of the scalp and hairy regions of the body often necessitates the examination of hairs. The standard method is to mount the hair in a 30 or even a 40 per cent solution of potassium hydroxide and let the mount stand for a few minutes. The application of a little heat hastens the clearing. It is advisable to dip the hairs taken from scalps, particularly those that are oily, in ether or in alcohol (absolute alcohol is preferable to 95 per cent alcohol) for a moment in order to get rid of the oil, which often simulates spores in shape and size.

Occasionally one has to examine a specimen for blastomycosis or torulosis. The presence of a double-contoured cell wall is of chief diagnostic interest, particularly in torulosis. In blastomycosis the wall is thick, the cell may be spherical, ovoid or budding and may be seen in a water mount. The organism of torulosis, *Cryptococcus histolyticus*, is

surrounded by a thick mucoid capsule and, unless distinguished by this characteristic, may be confused with the organism of blastomycosis. The method advocated by Weidman is the wet india ink technic. The suspected material is stirred in a drop of india ink, placed on a clean slide and covered with a cover slip. Care must be taken to work rapidly before the ink dries out. A small drop should be used so as to form a thin film. Against a dark background the capsule shows up as a clear halo surrounding the fungus. Spinal fluid may also be examined by this technic, although the background will not be as dark, owing to the dilution of the ink. Stains are not necessary for the organism, and they tend to spoil the effect of the ink.

These are but a few of the many technics in use. No doubt some prove more satisfactory than others to different dermatologists. A number of procedures not mentioned here may find greater favor with various technicians, but they require greater care, greater technical ability and a longer time for completion.

ISOLATION AND CULTIVATION OF THE PATHOGENS

When it has been proved by scraping or fluid mounts that a fungous infection is present, a culture should always be made. A number of mediums may be used, most of them, however, do not completely satisfy the requirements for the cultivation of a fungus. Nutrient mediums with a hydrogen ion concentration around the neutral point are generally to be avoided for isolation work, since the fungus grows comparatively slowly, if at all, and the nutrients form a good base for the growth of contaminating bacteria. This may be remedied in some mediums by the addition of a little lactic acid (85 per cent dilution of lactic acid U S P) to the sterilized medium before it has cooled. The acid hinders the growth of bacteria. If infection with filamentous fungi is suspected, a clear or light medium should be used because the pigment which is liberated by some fungi and diffuses through the medium is important in determining the classification of the organism. It is advisable to cleanse the lesion with 70 per cent alcohol to help rid it of contaminating bacteria. Strenuous methods should be avoided, for if they are employed the fungus on the surface may also be killed and the scrapings or scales may become useless for culturing. The material is then obtained and inoculated in the medium.

The most widely used and general medium for fungi is a modification of Sabouraud's original formula. This is prepared from 10 Gm. of peptone, 40 Gm. of dextrose, 15 Gm. of agar, and 1,000 cc. of tap or distilled water. The ingredients are dissolved by boiling for a few minutes while being stirred, dispensed in test tubes or other containers and sterilized at 120 pounds' (54.4 Kg.) pressure for twenty minutes,

the medium is then allowed to cool and if put in test tubes is slanted. The final medium has a p_H of about from 5.2 to 5.6. Maltose may be used in place of dextrose, but the latter is preferable for trichophytes in general. It is a clear substrate and allows for the distinguishing of diffused pigments. The original Sabouraud proof agar is made up with raw Chanut dextrose and granulated Chassaing peptone. These materials are difficult to obtain and are not always reliable as to purity or composition. It is therefore much better to adhere to a formula of definitely known constituents, such as the modification mentioned here. In addition to being clear the medium brings out markedly a number of cultural characteristics.

When the fungus has been grown on Sabouraud's modified maltose or dextrose agar and then studied, it is advisable, if the organism is to be maintained for purposes of teaching or of comparison, to grow it on a substrate that will not alter its morphology to any great extent or cause a loss of such anatomic features as spirals, fuseaux, characteristic spore formation and cultural appearance. A medium known as conservation agar is used. This, too, is a modification of Sabouraud's original constituents and is composed of the following ingredients: peptone, 30 Gm., agar, 15 Gm., and tap or distilled water, 1,000 cc. The principle involved centers around the lack of carbohydrate, the presence of which has an effect in changing morphology.

For the isolation of yeast Sabouraud's maltose agar has been used rather successfully. The best known medium, however, is wort agar, prepared by the following formula (Difco): maltose, technical, 12.75 Gm., malt extract, 15 Gm., dextrin, 2.75 Gm., glycerin, 2.35 Gm., di-potassium phosphate, 1 Gm., ammonium chloride, 1 Gm., peptone, 0.78 Gm. and agar, 15 Gm. When sterilized, the medium has a final p_H of approximately 4.7. A modified wort agar, malt extract agar (Difco), is not as efficacious as the wort agar.

One of the chief factors in the value of wort agar, in addition to its being a good substrate for yeasts, is its ability to eliminate almost entirely the growth of contaminating bacteria. This is due to its high hydrogen ion concentration which has no effect on yeasts but is harmful to bacteria.

There are a number of other mediums which may be used, some for isolation purposes and others for subculturing and propagating the fungus. These, however, should be left for the mycologist in his further work on the microbe.

STUDY OF THE FUNGUS AND ITS LIFE CYCLE

The important characteristics to be noted in the life cycle of a fungus are the development of the mycelium, the formation of the blastospores,

arthrospores and so-called oidiospores, the evolution and production of asci and ascospores, if present, and that of other mycelial structures, such as conidia, conidiospores, chlamydospores, hyphospores, sporangia and sporangiospores, penicilli, spirals, aleuriospores, fuseaux and racquet mycelium and several others

There are two main types of substrates to be used in carrying out these studies, the wet and the solid preparations. When the wet preparations are used the technic consists of the inoculation of a small amount of a liquid medium in such a way that the whole can be observed with a microscope. There are several ways of making these mounts, but those most commonly used are the van Tieghem cell, the concave slide and the Ranvier cell. The van Tieghem cell is probably the most commonly used. It consists of a collar of glass from 1.5 to 2 cm. in diameter and from 0.5 to 1 cm. in length, which is made to adhere to a glass slide either with Canada balsam (the oleoresin of fir) or some other adhesive. This forms a chamber, at the bottom of which it is advisable to place a drop of the medium to be used. A small drop of the liquid is also placed in the center of a cover slip large enough to cover the exposed edge of the glass collar which has been covered with sterile petrolatum or hydrous wool fat. The drop is then inoculated with the fungus, and the cover slip is inverted rapidly and placed on the glass collar. The cover slip is pressed down firmly so that it adheres tightly, with the petrolatum or hydrous wool fat acting as the adhesive. There is formed a relatively air-tight chamber from which the liquid medium will not evaporate readily.

In place of the van Tieghem cell, the depressed, concave slide may be used in much the same manner.

The third type of cell consists of a glass slide with a flattened oval depression. A deep groove surrounds the cavity. This is known as the cell of Ranvier. It is sealed in the same manner as the aforementioned slides. Its chief attributes are that when the depression is filled with the liquid medium, inoculated and covered, there is an extremely fine space between the cover slip and the slide, it is filled with liquid and is therefore much larger than a hanging drop, the germinating spore or fruiting body can be watched with ease. It surpasses the hanging drop further in that it does not require a great deal of focusing. In all these preparations all the materials should be sterile, and the manipulator should work rapidly to avoid contamination.

The liquid medium to be employed may be one of the usual broth substrates, such as nutrient broth, liquid wort (wort medium minus the agar), Sabouraud's medium minus the agar, 2 per cent peptone (bactopeptone, proteose or Witte's peptone), 2 per cent peptone plus 2 per cent dextrose or any special medium that may be desired. A

little glycerin may be added to a hanging drop medium. This is an added nutrient which keeps the broth from evaporating rapidly.

In place of the liquid a solid substance may be used. The medium is dissolved and a drop placed on a cover slip—in much the same manner as is the liquid drop—and inoculated before it has completely cooled. On the other hand, a small amount of the dissolved medium may be inoculated when it has cooled sufficiently not to kill the fungus and placed on the cover slip. A clear nutrient agar is always advisable. A clear nutrient or peptone medium with gelatin as a solidifier gives a transparent substrate. A better preparation, in place of the hanging drop culture, is made as follows. A drop of dissolved gelatinized medium is placed on a clean sterile slide, inoculated and covered with a sterile cover slip, which is pressed down firmly to allow only a thin space of gelatin between the cover slip and the slide, and the preparation is ringed with sterile petrolatum or hydrous wool fat or, preferably, paraffin.

It is often desirable to trace the change of a fungus from the parasitic to the saprophytic mode of life or to determine some phase of its cycle which is usually lost after subculturing. This can best be accomplished by mounting some of the scrapings, pus, sputum, spinal fluid or other material directly in medium, liquid or solid, by one of the aforementioned methods and then observing its evolution. This is particularly recommended for the yeasts and yeastlike organisms.

The further identification of a fungus, particularly a yeast, involves further biochemical reactions, such as liquefaction of gelatin, fermentation of carbohydrates, acidification and curdling of milk, and special features, such as spore production. Single spore cultures are also often necessary, but this involves special technic and the use of expensive apparatus and should therefore be left to one accustomed to this type of work. The materials and technics presented here, though not new and for the most part not original, should be sufficient for examination of the usual mycoses encountered by the dermatologist in his office.

Minor Notes

SUCCESSFUL TREATMENT OF RAYNAUD'S DISEASE WITH ESTROGENIC SUBSTANCE

EDMUND W. KLINEFELTER, M.D. YORK, PA

On Oct 30, 1935, a 34 year old, well developed and healthy-appearing woman, 5 feet, 3 inches (1.6 meter) tall and weighing 136 pounds (61.7 Kg), consulted me because of paroxysmal attacks of blueness, pain and numbness in her fingers. The history and physical examination disclosed that the patient had suffered from Raynaud's disease for the past seven years. During that time the attacks had progressed in severity, they disturbed the patient most at the time of menstruation, and she was comparatively free from discomfort during the intermenstrual interval. Usually a series of hot and cold flashes resembling menopausal hot flashes preceded an attack. The menstrual history was otherwise irrelevant except for the fact that a gradual diminution in the duration and amount of the flow had occurred in the past seven years. Laboratory studies revealed nothing of significance. The urine contained no albumin, sugar or hemoglobin. The Wassermann reaction of the blood was negative.

Examination during an attack showed that the hands became cold, blue and covered with sweat. The feet were only slightly involved. Pulsations were of good volume in both radial arteries.

The patient had received a wide variety of treatments, including administration of various tonics, and ammonium chloride, application of stimulating ointments and liniments, a ketogenic diet, contrast baths, Bier's hyperemia, galvanism, regular massage, dry heat and short wave diathermy. One physician advised injection into the sympathetic nerves or ganglionectomy.

For two months I prescribed large doses of calcium gluconate and ammonium chloride orally, but there was no improvement. Antipyrine, acetophenetidin and codeine, however, relieved the pain.

Since the paroxysms were associated with a menstrual disturbance and since the estrogenic substance not infrequently alleviates the hot and cold flashes of the menopause, 4,500 international units of estrogenic substance in oil was given intramuscularly on alternate days for seven doses. The medication was discontinued ten days before the onset of the menstrual period. A distinct improvement followed. The heat flashes and attacks of cyanosis in the fingers became markedly less severe. The periods lasted longer, and the flow became more free. After a repetition of the same treatment for two consecutive months the periods returned to normal, and all evidences of Raynaud's disease vanished. Since that time the patient has received no treatment. The periods have remained normal, and there have been no associated heat flashes or disturbances in the extremities.

COMMENT

Numerous reports appear in the literature indicating that in some cases a beneficial influence is derived from administration of estrogenic substance in the treatment of certain cutaneous diseases, but little reference is made to the use of this substance in the management of cutaneous diseases in which there is a conspicuous vasomotor component. Recently Drips and Brunsting¹ noted benefit from the administration of estrogenic substance in the treatment of urticaria, and

Janson² reported excellent results from its use in a case of severe axillary hyperhidrosis. A search of the literature, however, disclosed no report of a disorder such as that which I have described in which benefit followed the use of estrogenic substance.

546 West Market Street

1 Drips, D G, and Brunsting, L A. Urticaria and Endocrine Dysfunction, Proc Staff Meet, Mayo Clin. 10 764 (Nov 27) 1935

2 Janson. Schwere Hyperhidrosis axillaris und deren Heilung durch Progynon, Med Klin 32 121 (Jan 24) 1936

TREATMENT OF PAINFUL SITES OF INJECTIONS

LESTER HOLLANDER, M D, AND JOSEPH M SHELTON, M D, PITTSBURGH

In a few cases ultrashort wave therapy was used for the alleviation of pain following intramuscular injections or the use of sclerosing agents for various ulcers. The result was so satisfactory that this brief communication is made in the hope that others may avail themselves of this form of therapy. The apparatus used was a 6 meter ultrashort wave appliance with glass electrodes, the length of exposure was ten minutes, and treatments were repeated every second day.

Four patients with pain at sites of injections of a bismuth preparation received two treatments each according to this method, complete disappearance of pain resulting in the four instances, two patients with severe pain from injections into varicose veins received five treatments each, complete relief from pain resulting. In one patient with pain due to injection of histidine hydrochloride who received only one treatment satisfactory results likewise occurred.

631 Jenkins Building

From the Pittsburgh Skin and Cancer Foundation

TREATMENT OF ERYTHEMA INDURATA (BAZIN'S DISEASE)

ANDREW L GLAZE, M D, BIRMINGHAM, ALA

The treatment of erythema indurata (Bazin's disease) is not quite satisfactory.

In a young woman with the nonulcerative form of this disorder, which proved unresponsive to the usual constitutional remedies and measures, apparent complete relief with rapid resolution of the infiltrations in the hypodermis followed daily application for three weeks of a mixture of equal parts of collodion U S P and flexible collodion U S P. The affected areas and the sound skin for some distance around were painted with the mixture. Each new application was made over the previous ones. The almost startlingly favorable result appeared to have come about as a result of local splinting of the parts from the continuous contractile action exercised by the topical agent.

News and Comment

PROGRAM NOTICE, ATLANTIC CITY MEETING OF AMERICAN MEDICAL ASSOCIATION

Applicants for a place on the program of the Section on Dermatology and Syphilology of the American Medical Association at the meeting in Atlantic City, N J, from June 7 to 11, 1937, are requested to submit titles and provisional abstracts of their proposed papers to the secretary of the section, Dr Bedford Shelmire, Medical Arts Building, Dallas, Texas

Applicants need not be members of this section but must be Fellows of the Association, graduates in medicine not in private practice or invited guests

Correspondence

USE OF TRYPARSAMIDE IN PRIMARY STAGES OF SYPHILIS

To the Editor—I wish to correct a seemingly serious ambiguity in my recently published paper on tryparsamide (ARCH DERMAT & SYPH 34:582 [Oct] 1936). It appears that certain of my colleagues are laboring under the impression that I am advocating the use of tryparsamide alone in the primary stages of syphilis. This interpretation is as incorrect as it is difficult to understand, for in the summary of the aforementioned article I stated that tryparsamide has but a mediocre effect in suppressing early lesions. Indeed, the small amount of work done with the drug in cases of primary syphilis (two cases) indicates only too well that at the time the report was made the work was in the nature of an experiment which was undertaken with no small degree of trepidation. I merely advocated that tryparsamide be incorporated into the curriculum of the Cooperative Clinical Group as outlined for early antisyphilitic therapy in the hope that tryparsamide might have some effect in reducing the ultimate incidence of neurosyphilis. My plan was to use tryparsamide on alternate weeks during the phase of treatment with heavy metals.

H SUTHERLAND-CAMPBELL, M D
1930 Wilshire Boulevard,
Los Angeles

Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

COMPARATIVE CHEMOTHERAPEUTIC STUDIES OF "ARSENOXIDE" (3 AMINO-4-HYDROXY-PHENYL-ARSENIOXIDE) AND NEOARSPHENAMINE G W RAIZISS and M SEVERAC, Am J Syph & Neurol 19 473 (Oct) 1935

Recently the attention of syphilologists has been called again to arsenoxide as an antisyphilitic agent. The authors made an experimental study of the toxicity and therapeutic efficiency of arsenoxide as compared with that of neoarsphenamine. As a result of their investigations they conclude that neoarsphenamine is far superior to arsenoxide in both trypanocidal and spirocheticidal properties. In rabbits with experimental syphilis the maximum tolerated dose and the minimum curative dose of arsenoxide are practically identical, this suggests that the clinical use of this drug in adequate curative doses may be fraught with considerable danger.

A PRELIMINARY STUDY OF THIO-ARSENE, DISODIUM BIS-(P-SULFOPHENYL) (ACETAMIDOPHENYL)-DITHIO-ARSENITE. C R ECKLER and H A SHONLE, Am J Syph & Neurol 19 495 (Oct) 1935

Over twenty compounds comprising combinations of over eight arsenoxides with five thio-acids were studied. The substance finally selected for clinical study was di-sodium bis (para-sulfophenyl) (acetamidophenyl)-di-thio-arsenite. It is a definite chemical substance containing 11.88 per cent arsenic. When dry, it is stable in air. In the absence of air aqueous solutions have been kept without deteriorating for one and a half years. Oxidized solutions have proved to be less toxic than the original solutions. The toxicity of this drug is lowered by the addition of sodium para-thiophenyl sulfonate, and there does not appear to be any loss of trypanocidal effectiveness when both are given.

In clinical and experimental work a stable solution in ampules has been used, each cubic centimeter containing 0.025 Gm of di-sodium bis (para-sulfophenyl) (acetamidophenyl)-di-thio-arsenite and thiophenyl sulfonic acid to the extent of from 225 to 275 times the weight of the former. Sufficient mono-ethanolamine is then added to give the solution a p_H between 8 and 9.2.

Trypanocidally di-sodium bis (para-sulfophenyl) (acetamidophenyl)-di-thio-arsenite is twice as potent as arsphenamine, weight for weight. The drug is excreted largely by the kidneys and intestines. In human beings most of the arsenic given may be recovered by the end of five days. The average spirocheticidal potency of the drug in ampules is 206 mg per kilogram, while the potency of arsphenamine is 15 mg per kilogram. However, on the arsenic basis the arsenic in the former is at least twice as potent as the arsenic in the latter.

CLINICAL OBSERVATIONS ON THE TREATMENT OF SYPHILIS BY A COMBINATION OF BISMUTH SALICYLATE AND A NEW ARSENICAL SYNTHETIC S W BECKER and M E OBERMAYER, Am J Syph & Neurol 19 505 (Oct) 1935

This report concerns a clinical study of a new arsenical synthetic drug, di-sodium bis (para-sulfophenyl) (acetamidophenyl)-di-thio-arsenite, used in combination with bismuth subsalicylate in the therapy of syphilis. About 4,000 injections have been given 291 syphilitic patients during the past three years.

The drug when administered with bismuth subsalicylate acts less rapidly, clinically and serologically, than arsphenamine used in the same way, but late relapses following combined treatment did not occur in Becker and Obermayer's series of 291 patients. Reactions consisting of nausea, vomiting and diarrhea occurred after from 20 to 30 per cent of the total number of injections given.

Retarding the rate of injection reduced the reactions by more than 50 per cent. Jaundice developed in 8 of 291 patients, all recovered. Dermatitis and hemorrhagic accidents were not encountered.

Becker and Obermayer believe that their experience entitles the drug in combination with bismuth subsalicylate to serious consideration in syphilotherapy.

THE THERAPEUTIC VALUE OF THIO-ARSENE. A CLINICAL STUDY OF THE THERAPEUTIC EFFICIENCY AND TOXICITY OF DISODIUM BIS-(P-SULFOPHENYL) (ACETAMIDOPHENYL)-DITHIO-ARSENITE, BASED ON 2,282 INJECTIONS ADMINISTERED TO 251 PATIENTS WITH SYPHILIS. W. H. CONNOR, H. C. SHAW, E. A. LEVIN and R. B. PALMER, *Am J Syph & Neurol* **19:514** (Oct.) 1935

The authors found that di-sodium bis (para-sulfophenyl) (acetamidophenyl)-di-thio-arsenite does not possess a high degree of therapeutic efficiency even when administered biweekly in the highest tolerated doses. From their clinical study they conclude that the drug is probably not suitable for the treatment of syphilis, especially since more efficient and better tolerated preparations are available.

THE TREATMENT OF SYPHILIS WITH A NEW ARSENICAL DRUG. H. M. ROBINSON and J. E. MOORE, *Am J Syph & Neurol* **19:525** (Oct.) 1935

This paper presents the results of another clinical study of the new arsenical compound di-sodium bis (para-sulfophenyl) (acetamidophenyl)-di-thio-arsenite in the treatment of early stages of syphilis. The drug was employed alone, no other form of antisyphilitic treatment being given.

This preparation produced gastro-intestinal reactions in such a large proportion of cases even when the advised dose was reduced that many patients were unwilling to submit to continued treatment with it. The drug is not utilizable in treatment of patients who have previously been sensitized to the arsphenamines. It provoked a fresh dermatitis in seven of eleven patients thus sensitized.

As to therapeutic efficacy the preparation compares unfavorably with any of the arsphenamines or with bismuth preparations in its effect on the disappearance of surface organisms in open lesions, on the healing of lesions and on the Wassermann reaction of the blood.

Robinson and Moore conclude that the drug in its present form is not entitled to serious consideration in syphilotherapy.

REUTER, Milwaukee

HEREDITARY ECTODERMAL DYSPLASIA OF THE "ANHYDROTIC TYPE." S. J. THANNHAUSER, *J. A. M. A.* **106:908** (March 14) 1936

The symptomatic triad of this malady consists of complete inability to sweat, a deficiency of scalp, axillary and pubic hair, and incomplete development of the teeth. Other findings in most instances include saddle nose, a decrease in the intellect and a deformity of the auricles. In some cases only the hair and nails are affected. Usually a definite hereditary factor is present, the transmission being recessive and obligatory to the male sex. In the case reported by Thannhauser the patient had a pedigree confirming the fact that the transmission was recessive and obligatory to sex. He did not perspire until his sixteenth year. There were signs of insufficiency of the adrenal medulla, and the roentgenograms of the skull showed bony deformity.

HISTORY TAKING IN ALLERGIC DISEASES. FRANCIS M. RACKEMANN, *J. A. M. A.* **106:976** (March 21) 1936

In allergic diseases, the history is the chief diagnostic measure. Rackemann advises that a careful history should include all the ordinary questions usually related to a diseased state. Particularly important, however, in obtaining a history of a patient with eczema or other allergic disease, are (1) the family history and (2) the particular history of the complaint. The latter should include exact dates and not casual time periods. It is necessary to account for all the

time, both during an attack and during periods in which the patient is free from the disturbance. It is also important to trace the effect of change of residence, occupation, habits, diets, etc. Elimination of suspected allergens, both in the diet and in the surroundings, may be an important diagnostic procedure. Rackemann states that dusts as well as foods may cause atopic eczema.

ARGYRIA BECOMING MANIFEST IN PREGNANCY JOHN RAAF and H K GRAY,
J A M A 106.916 (March 14) 1936

Raaf and Gray report the case of a woman who fifteen years before underwent a tonsillectomy and during the next five years used a throat spray containing mild protein silver twice a day. Near the end of that five year period she gradually discontinued the practice, and for six months before the beginning of a pregnancy (nine and a half years before she was seen by Raaf and Gray) she had not used the spray. In the first month of the pregnancy a discoloration appeared and gradually spread over the entire body, and it has remained unchanged since that time. The clinical diagnosis was confirmed by the finding of silver granules in the gallbladder and appendix, which were removed at operation. The deposition of silver in the skin is thought to have been due to a disturbance in metabolism attributable to pregnancy.

THE ANTERIOR PITUITARY-LIKE HORMONE. A CLINICAL STUDY OF ITS EFFECTS IN ACNE VULGARIS CHARLES H LAWRENCE, J A M A 106 983
(March 21) 1936

Although further study is necessary to determine the exact nature of the endocrine imbalance, investigations point to a dysfunction in either the gonads, the pituitary gland or both as a cause of acne vulgaris. Thirty patients with acne were treated by means of injections of 2 cc of the gonadotropic hormone of the urine of pregnant women (antuitrin-S) every other day. Ten patients were regarded as cured, and eleven others were much improved.

TULAREMIA HAROLD L AMOSS and DOUGLAS H SPRUNT, J A M A 106
1078 (March 28) 1936

Amoss and Sprunt report on two patients with tularemia in whom infection developed after ingestion of a rabbit. It was assumed that the rabbit was not well cooked. In the first patient the onset of the disease occurred about eight hours after he had eaten part of the rabbit. The disease was ushered in with pain in the left side of the chest and a severe chill, later gastro-intestinal symptoms and high fever ensued. Shortly thereafter the patient became stuporous and irrational. The course of the disease was steadily downward until death, which occurred thirteen days after the onset. Agglutination for *Bacterium tularense* was positive in a 1:640 dilution of serum. The anatomic diagnosis was tularemia, there were focal necrosis in lymph nodes and in the spleen and lungs, focal accumulation of round cells in the liver, interstitial monocytic pneumonia, lobular pneumonia and pulmonary emphysema. In the second patient, who ate part of the same rabbit as the first patient, a similar series of events and a fatal outcome also occurred. In this patient, however, repeated agglutination tests of the blood for *Bacterium tularense* gave negative results. Only three other cases have been reported in which tularemia developed from the ingestion of diseased rabbits.

THE SUBCUTANEOUS INJECTION OF ALCOHOL FOR PRURITUS ANI BENJAMIN HASKELL and CLARENCE D SMITH, J A M A 106 1248 (April 11) 1936

Haskell and Smith advocate the subcutaneous injection of alcohol for the relief of pruritus ani. They found that in a series of twenty-two patients, observed for a year or more, sixteen obtained complete relief, four remained com-

fortable, and two failed to obtain relief. Only small segments of perianal tissue were treated at one time. A 2 per cent solution of procaine hydrochloride was used to prevent pain during and after the injection. From 3 to 5 cc of a 70 per cent solution of ethyl alcohol was injected at one time, care being taken not to harm any of the deeper tissues. From two to six such injections were required. The only complication encountered was slight sloughing, which occurred in six of the twenty-two patients.

LEWIS, New York

CONTROL OF PIGMENT MIGRATION WITHIN THE CHROMATOPHORES OF *PALAEMONETES VULGARIS* F A BROWN JR, J Exper Zool **71:1** (July 5) 1935

All the movements of the pigments within the chromatophores of the shrimp, *Palaemonetes vulgaris*, are controlled by hormones, and each pigment is controlled by an independent hormone. Concentration of the white pigment is produced by a hormone formed in the eyestalks and in some tissue of the anterior region of the cephalothorax. Concentration of the red and the yellow pigments is produced by hormones formed in the eyestalks and in the central nerve organs. There is some evidence that a hormone is contained in the eyestalks which controls the blue pigment. Dispersion of the pigments may be explained by the absence of the pigment-concentrating hormones. The eyes are the only receptors involved in the responses of the chromatophore system of *Palaemonetes*.

WYMAN, BOSTON [ARCH NEUROL & PSYCHIAT]

SYPHILIS AND MENTAL DISEASES WILLIS E MERRIMAN, J Social Hyg **21:164** (April) 1935

During the year ending June 1933, syphilis was considered a causative factor in the cases of 11.3 per cent of all new patients admitted to the civil state hospitals. In 1931 Pollock computed the annual economic loss resulting from mental disease due to syphilis in the state of New York as approximately \$13,500,000. The incidence of dementia paralytica in that state is nearly three times as great in cities as in rural districts when the estimate is based on respective urban and rural populations. Of over 16,000 patients with dementia paralytica admitted to the state hospitals during two recent decades, 13,000 died within an average of less than two years after admission. Modern methods of treatment have proved to have a decided advantage over earlier ones, but apparent recoveries are secured only in a distinct minority of cases.

FERGUSON, Niagara, Falls, N Y [ARCH NEUROL & PSYCHIAT]

HEREDITARY ECTODERMAL DYSPLASIA OF THE ANHIDROTIC TYPE WITH REPORT OF TWO CASES EDWIN G SCHWARZ, South M J **28:606** (July) 1935

The authors report two cases of hereditary ectodermal dysplasia of the anhidrotic type. This rare condition is apparently always hereditary. The defects are developmental anomalies involving structures of ectodermal origin, and patients with this disorder are unable to perspire. The skin, together with the sweat glands and sebaceous glands, the nails, hair and teeth, the external organs of special sense, the nervous system and the mucous membranes of the mouth, nose and anus, are involved.

One of the children was 8 years old and the other 6.

The etiology is undetermined. Although children with this disease commonly show pronounced saddle nose, syphilis is usually not an etiologic factor. The same is true of tuberculosis. No positive endocrinopathy has been found, although many patients have been given thyroid extract because of the condition of the hair, nails and skin. There seems to be no effective treatment for the condition.

SCHLUTZ, Chicago [AM J DIS CHILD]

BIOLOGICAL THERAPY IN VIRUS DISEASES R T BRAIN, *Brit J Dermat* 48.21 (Jan) 1936

Brain reports five cases of recurrent herpes treated successfully with specific vaccine. In general, the interaction of virus and specific antibody can be demonstrated by such reactions as complement fixation, agglutination, precipitation and neutralization. In the work on complement fixation a 10 per cent suspension of herpetic pads from guinea-pigs proved to be a satisfactory antigen, and such a suspension inactivated with an 0.08 per cent solution of formaldehyde in saline solution was used for specific vaccine therapy. Brain briefly considers the subject of immunity in diseases caused by a virus and the rationale of biologic therapy. He suggests that the failure to cure molluscum contagiosum and warts by vaccines may be due to the fact that the intracellular virus is protected from circulating antibodies by the selective nature of the cell membrane.

A CASE OF DERMATITIS VENENATA DUE TO MANSONIA WOOD (TERCULIACEA ALTISSIMA) SYBIL HORNER and J E M WIGLEY, *Brit J Dermat* 48 26 (Jan) 1936

The patient had been a wood-worker (sawyer) in a factory for twenty-five years and had never had any cutaneous eruption until shortly after he began to work with "mansonia walnut," a wood imported from Nigeria.

CHEILITIS ASSOCIATED WITH MICROCYTIC HYPOCHROMATIC ANEMIA BEATRICE LEWIS, *Brit J Dermat* 48 32 (Jan) 1936

A woman aged 49 had intractable cheilitis of two years' duration. She was also found to have pallor of the skin and mucous membranes, atrophic glossitis and koilonychia of all the finger-nails. Examination of the blood showed microcytic hypochromatic anemia. The presence of spoon nails was thought to be of great diagnostic significance, and the cheilitis was regarded as an unusual manifestation.

RATTNER, Chicago

FUNCTION OF THE PIGMENT IN THE SKIN ROBERT AITKEN, *Brit J Phys Med* 10 30 (June) 1935

Experimental work is presented to show that pigment in the skin serves as a defense against luminous rather than against ultraviolet radiation.

HARTMAN, Cleveland [AM J DIS CHILD]

LEUKAEMIC INFILTRATIONS J BURTON CLELAND, *Brit M J* 2:1191 (Dec 21) 1935

This article, written by a pathologist, discusses the various types of infiltration of tissue with leukemic cells. The infiltrating cells probably reach their location by way of the blood stream and subsequently multiply there. The infiltration is, however, more diffuse than that of an ordinary malignant embolus. Death is usually caused in these cases by secondary anemia and intercurrent infection. In some cases when the kidneys are intensely infiltrated death may result from uremia or from hemorrhage in the brain. Cleland points out that the enlargement of the spleen is not essential in order to arrive at a diagnosis of leukemia and reports several cases.

A man aged 57 died suddenly, exhibiting signs of acute cardiac failure. Post-mortem examination showed infiltration of the cardiac muscle and of the tubules of the kidneys by round cells. There was also a large amount of fluid in the pericardial cavity. The liver and spleen were not infiltrated.

A man aged 42 died of severe anemia, dilatation of the heart and early hypostatic pneumonia. Microscopic examination showed round cell infiltrations, with some myelocytes, in the septum and papillary muscle of the heart. The liver also showed a similar infiltration.

A 12 year old school boy died in a "fit" shortly after having been struck on the head by a cricket bat or ball. Postmortem examination showed a large liver and a large spleen, and in sections of the brain there were extensive areas packed with cells of a myeloblastic or myelocytic type. The kidneys and liver were diffusely infiltrated.

An 18 months old child died of a sloughing ulceration of the pharynx, and postmortem examination showed extensive infiltration of the kidneys with myelocytic cells. The pancreas and thymus were also extensively infiltrated.

In the first three cases there was no indication of the leukemic nature of the disease before death.

In 3,500 postmortem examinations Cleland found evidence of the following diseases: myeloid leukemia, 9 cases, myeloblastic leukemia, 4 cases, ordinary lymphatic leukemia, 7 cases, lymphatic leukemia with extensive infiltration, 3 cases, aleukemic leukemia, 3 cases, leukemic infiltration, 4 cases (no blood counts were made in these cases), possible leukemia (atypical), 3 cases, lymphosarcoma, 6 cases, multiple myeloma, 2 cases, chloroma, 1 case, ordinary Hodgkin's disease, 7 cases, acute Hodgkin's disease, 6 cases, Hodgkin's disease with sarcoma, 3 cases.

Four cases of proved leukemia with infiltration are described.

In 1 case there was infiltration of the liver and kidneys with myelocytes and mitoses. In another there were infiltrations at the sites of injections with soamin (sodium para-aminophenylarsonate) and at the site of a surgical incision. In a third case there were lymphatic leukemia, tumor-like infiltrations and nodules in the kidneys, liver and pericardium and plaques on the ribs and spinal canal. In 1 case of lymphatic leukemia there were tumor-like masses around the abdominal aorta, kidneys, mediastinum and left scrotal sac.

In 2 of the cases studied by Cleland there were infiltrations of viscera, in 1 case this was associated with a low and in another with a normal white cell count. Cleland also gives several examples of lymphosarcomatosis and states that no sharp line of demarcation exists between this condition and pseudo-leukemia.

This article is illustrated with several photomicrographs of the cellular infiltrations.

APPEL, Boston

ACRODYNIA AND AVITAMINOSIS MALDAN-MASSOT, *Bull Soc de pédiat de Paris* 31:460 (Nov) 1933

A girl 21 months old presented a typical picture of acrodynia. She had been fed nothing but milk and pap. Vegetables, meat juice, calf liver and lemon juice were added to the diet, and after three days the child was markedly improved. On the eighth day from the time she was first observed, administration of 20 drops of a preparation of vitamins A and D and the use of thyroid and adrenal extracts were added to the daily regimen. At the end of a week the child was again examined, and only tachycardia remained of all the signs that were present when she was first observed. The case is reported as an instance which lends weight to the theory that acrodynia is a deficiency disease.

CASE OF RELAPSING ACRODYNIA. STUDIES OF THE VASOMOTOR SYNDROME B WEILL-HALLÉ and BORIS KLOTZ, *Bull Soc de pédiat de Paris* 32:447 (July) 1934

A boy 13½ years old presented a typical picture of acrodynia. Most of the cases of this disease which have been reported occurred in much younger children. The patient had marked subconjunctival hemorrhages, without any evidence of other hemorrhage in the body. This case is considered to be the first instance of acrodynia in which this manifestation was present. Another point of interest is that the boy had acrodynia about ten years before, which took about nine months to heal. The duration of the second attack of acrodynia was five months. Injections of acetylcholine and ultraviolet irradiation were used in treatment. These measures

are considered to be of benefit in the treatment of this disease. The sugar, urea and calcium contents of the blood and the sedimentation velocity were normal. Interferometric examination gave normal values for the thyroid and the posterior lobe of the pituitary gland but values higher than normal for the anterior lobe of the pituitary and the thymus, testicle and adrenal. The fact that the boy was at puberty may have influenced these results. The vasomotor system was studied. The peripheral capillaries showed no anatomic abnormalities, but there was functional disturbance. More than the normal number of loops could be seen, and there were stasis and dilatation at the bottom of the loops. The arterial pressure in the retina was found to be elevated during the disease and to be normal later, when the boy had recovered. The oscillometric index was low for all the extremities, and the reactions to heat and cold were abnormal, after the injection of large doses of acetylcholine the index was exceptionally high. Intravenous injection of atropine demonstrated hypersympathicotonia and slight hypovagotonia. In this case definite vasomotor disturbance was shown, as evidenced by stasis of the peripheral capillaries of the extremities and arterial vasoconstriction, associated with hypersympathicotonia. Manifestations of this disturbance were observed as tachycardia, hypertension, especially of the diastolic type, a very low oscillometric index and paradoxical response to immersion of the extremities in a hot bath.

THREE CASES OF MALFORMATION OF THE SKIN OF THE NECK. LATERAL FOLDS OF THE SKIN (PTERYGIUM COLLI CONGENITUM), LATERAL AND POSTERIOR FOLDS AND SUBMAXILLARY DERMATOPTOSIS. Mlle NAGEOTTE-WILBOUCHE-VITCH, *Bull Soc de pediat de Paris* 32 683 (Dec) 1934

These observations were made on three women, two aged 19 and one of advanced years and married. None had any abnormality of the vertebrae, although no mention is made of roentgenologic examination. It is believed that the abnormality of the skin of the neck does not appear as a single congenital deformity but is only part of a disturbance probably of endocrine origin. Other abnormal characteristics may be present, such as infantilism, obesity, amenorrhea, congenital defects of the heart, anomalous development of the hair, cutaneous folds on the shoulders and elbows, excessively large ears and various malformations of the face and limbs, all of which may be due to an endocrine disturbance.

BENJAMIN, Montreal, Canada [*AM J DIS CHILD*]

ERYTHRODERMA DESQUAMATIVUM (LEINER-MOUSSOUS DISEASE). P LEREBoullet and A BOHN, *Nourisson* 23 201 (July) 1935

This report concerns eighteen cases of erythroderma which occurred within a few months among the infants in a hospital for foundlings near Paris. The average duration of the disease was from one to two months, and in no case did a chronic type of infantile eczema result. In a few instances cutaneous abscesses developed as a complication. One patient died of bronchopneumonia. The disease appeared only in infants who were fed artificially. Laboratory investigations showed an excessive number of enterococci both in the stools and in the desquamations of the skin of the babies with the disease. This may be of etiologic significance, though it does not explain why all the cases occurred on one floor of the hospital. Practically all the babies with the disease failed to gain weight normally, and marked anemia developed. Treatment is not discussed.

McClelland, Cleveland [*AM J DIS CHILD*]

A CASE OF DERMATOMYOSITIS. OLEA G RICARDO, *Arch Hosp de Niños Roberto del Rio* 5 78 (June) 1935

The author reports the rare condition of dermatomyositis in a child over 3 years old. The chief symptoms were swelling and bleeding of the gums and painful swellings about the elbow joints and in the knees and calves of the legs. Considerable edema and erythema developed about the mouth and over the involved

areas of the extremities. Ricardo states that contractures in the extremities are a sequel occasionally. The prognosis is generally good. There is no specific treatment. A diet with high vitamin content is recommended.

SCHLUTZ, Chicago [AM J DIS CHILD]

INFLUENCE OF THE SPLEEN ON ALLERGIC CONDITIONS C R GRIEBEL, Arch f Ohren-, Nasen- u Kehlkopfh 140:101, 1935

Griebel reviews the literature on the functions of the spleen and describes his studies of its influence on allergic conditions. He made sugar tolerance tests on rabbits, some of which had first been sensitized by repeated subcutaneous injections of small amounts of an allergen. The allergic animals showed considerable eosinophilia. In tolerance tests it was proved that the metabolism of sugar is disturbed in these animals in that the sugar content of the blood reaches an unusually high level and remains at this high level for much longer periods than it does in animals that have not been made allergic. However, when the allergic animals were given an injection of an extract of spleen (free from protein, sugar and lipoid) before undergoing the sugar tolerance test the reaction was considerably reduced toward the normal. In other experiments the reticulo-endothelial system of the animals was blocked. Griebel concludes that clinical observations as well as experiments on animals indicate that the spleen exerts a considerable influence on the eosinophilic blood picture. It was found that the administration of an extract of spleen in allergic disturbances (bronchial asthma, vasomotor rhinitis and hay fever) produces the best results in vasomotor rhinitis, in hay fever the effects are less favorable, and in bronchial asthma they are least favorable. To be sure, the eosinophilia was reduced in all these conditions, but only in vasomotor rhinitis was this reduction accompanied by a cure. Griebel considers spleen therapy promising in the treatment of allergic disorders.

EDITOR'S ABSTRACT [ARCH OTOLARYNG]

THE TREATMENT OF TUBERCULOSIS OF THE MUCOUS MEMBRANE O WARTEMAN, Dermat Wchnschr 100:680 (June 15) 1935

Wartemann reports good results in the treatment of tuberculosis of the buccal mucosa by means of moderate diathermy followed by painting with a combination of two complex preparations, the first containing calcium carbonate, potassium phenolate and phenol and the second containing salicylic acid, sodium silicate, glycerin, sugar and spermaceti.

CUTANEOUS AND ORGANIC DISEASE AS LATE SYMPTOMS OF INFECTIONS DEZSO VON KÉMERI, Dermat Wchnschr 101:939 (Aug 3) 1935

The author discusses the importance of focal infection in relation to cutaneous disorders. Focal infection may cause, or affect the course of, many different conditions, some of which are considered specific.

IMPREGNATION OF THE SKIN WITH ZINC I I POTOTZKI, Dermat Wchnschr 101:947 (Aug 3) 1935

A 32 year old man received a blow near the eye in the course of a fight. The denuded area was dressed with a paste containing zinc which was allowed to remain for twenty-five days. Subsequently multiple white spots were seen in the skin, each surrounded by a telangiectatic network. Chemical investigation showed that the spots were zinc.

ANOTHER CASE OF SYPHILITIC CHANCRE PRESENTING THE PICTURE OF BALANITIS (BALANITIS SPECIFICA SYPHILITICA FOLLMANN) FERDINAND GERENCSE, Dermat Wchnschr 101:976 (Aug 10) 1935

A case is described in which the chancre was clinically suggestive of balanitis simplex.

CLINICAL OBSERVATIONS ON LEPROSY AND ITS TREATMENT PETER SUMMENT,
Dermat Wchnschr 101 1002 (Aug 17) 1935

Summent expresses the belief that leprosy is more common in Europe than is generally believed, especially in Estonia and in Lithuania. He comments on the fact that the method of transmission of the disease is still unknown. In the treatment of leprosy, the usual derivatives of chaulmoogra oil are used. In addition resistant ulcers have been successfully treated with a powder of sulfur and tar.

THE VARICOSE SYMPTOM COMPLEX WILHELM RICHTER, Dermat Wchnschr 101 1023 (Aug 24) 1935

Richter reviews the "varicose symptom complex" with its various cutaneous manifestations. He also discusses the local and general treatment.

ECZEMA AND HEMOLYTIC JAUNDICE. A. W. DAWIDOW, Dermat Wchnschr 101 1030 (Aug 24) 1935

A 42 year old man entered the clinic for treatment of an eczema which had been present on the face and extremities, showing exacerbations, for twenty years. On examination hemolytic jaundice was found to be associated with the eczema.

A SIMPLE METHOD FOR THE REMOVAL OF TATTOOING G. H. KLOVEKORN, Dermat Wchnschr 101 1271 (Oct 12) 1935

Klovekorn refers to Janson's article (*Dermat Wchnschr* 101 894 [July 20] 1935) and states that two or three years ago at a clinic in Cologne a patient had a tattoo removed without a scar. The method employed was the daily massage with moistened sodium chloride. The author treated another patient successfully by the same method. The area was rubbed until it became erythematous, and it was necessary to continue this treatment for several months.

TAUSSIG, San Francisco

FROM "ACRODYNIA" TO "ENCEPHALITIS VEGETATIVA," THE HISTORY OF A DISEASE
PAUL SELTER, *Ergebn d inn Med u Kinderh* 46 315, 1934

Except for the epidemic of acrodynia which occurred in France from 1828 to 1832, the author claims to have first called the attention of the medical world to this disease in 1903, when he described eight cases, designating the condition as "trophodermatoneurosis." The disease is the result of infectious or postinfectious damage of the central nervous system, with striking involvement of the ectoderm and its derivatives.

First, the hands and feet redden and swell, the disorder simulating first degree frost-bite, and this is followed by gross desquamation. The redness involves not only the hands and feet but practically all the terminal parts of the body, such as the nose, ears, cheeks and external genital organs. Sometimes this is preceded by a transient initial exanthem of scarlatiniform, morbilliform or urticarious character. Considerable sweating, unrelated to the intensity of the disease, is a rather constant finding. Paresthesias of all sorts, ranging from anesthesia to hypesthesia and hyperesthesia of a degree which "burns like fire," have been observed by various clinicians. The hair and nails show nutritional disturbances, the hair becomes brittle, dry and lusterless and may change in color, while the nails may break off near the edges and, after the termination of the illness, may show striations similar to the changes following acute infectious diseases, such as scarlet fever. Rarely, the nutritional disturbances of the skin, manifested by the wet, cold and cyanotic extremities, may lead to necrosis or even to gangrene, indicating that one is dealing in this disease with trophic disturbances. Excessive salivation, loss of teeth, occasional vomiting, diarrhea, anorexia, thirst, epigastric pain, hypersecretion from the nose and eyes, the occasional development of keratitis, frequent and marked photophobia, bronchitic phenomena and disturbances of the urine are all symptoms

resulting from involvement of the tissues that are derived from the "ectoblast" The palsy is not complete It is manifested by fatigue and pain in the extremities, and the patient walks like one suffering from progressive muscular dystrophy The condition is not true palsy but hypotonia of the muscles The reflexes may be normal, increased or diminished, similarly, the electrical reactions may vary from one case to another The circulation of the blood, not the circulatory organs or the blood elements, is disturbed, giving rise to tachycardia as well as to an increase in the blood pressure Various other disturbances, such as delirium, attacks of cramplike pain, inability to talk and apathy followed by excitability, crying, insomnia, restlessness and a host of other functional irregularities, are observed at various stages of the disease The temperature is usually normal and may be subnormal, when a complicating infection sets in, the temperature is, of course, elevated As a result of the anorexia and vomiting, most patients lose considerable weight The laboratory studies yield negative results The author states that the pathologic observations are similar to those of encephalomyelitis The course of the disease varies from three weeks to three years, the usual duration being from two to three months Most patients recover, the mortality being somewhere between 5 and 6 per cent The author concludes that the disease is an infection causing injury of the "vegetative cerebral centers," and he therefore calls the disease encephalitis vegetativa CAPPER, Philadelphia [AM J DIS CHILD]

CASES OF VEGETATIVE NEUROSIS (FEER'S DISEASE) T VARGA, Orvosi hetil
79:379 (April 6) 1935

Three cases are reported The first child, aged 3 years, had severe itching of the palms and soles, so that they had to be scratched with a brush, even in the night, and the child could not sleep because of the itching Other symptoms were also found, such as acrocyanosis, excessive perspiration, hypotonia, decrease of the reflexes, etc The second child, aged 4 years, had the same symptoms, but the itching was not as severe as in the first case The third case was that of a 10 year old girl The illness began with fever, which lasted one week The typical symptoms of Feer's disease were also to be found, but the mental depression and the disorders of motion and sleep pointed to encephalitis It seems that there are borderline cases, in which the condition forms a transition between Feer's disease and encephalitis

GOTTCHÉ, Budapest, Hungary [AM J DIS CHILD]

PATHOGENESIS OF IMPETIGO CONTAGIOSA ALBOSTAPHYLOGENES (DOHI) H ASANO,
Jap J Dermat & Urol 38:792 (Nov) 1935

A vesicular eruption consisting of single or multiple translucent, flaccid vesicles from the size of a millet seed to that of a cherry with a meager surrounding inflammatory reaction or none is frequently encountered during the warm, humid months in Japan It has been studied by the Dohis and others and ascribed to *Staphylococcus albus* In the relatively few cases in which *Staphylococcus aureus* has been the organism encountered it has been dismissed from consideration as merely a secondary invader or part of a mixed infection

Asano, however, secured *Staph. aureus* in pure culture in 21.4 per cent of a group of cases of this disorder By means of parallel studies of *Staph. albus* and *Staph. aureus* as to biologic characteristics (coagulation of milk, fermentation of sugars, hemolytic power, culture on crystal violet mediums, agglutination reaction, resistance to acid and to heat, behavior toward antiseptics, such as acriflavine hydrochloride, an acridine derivative and glycerin, toxicity when injected intraperitoneally into rats and toxicity for the skin of rabbits, of guinea-pigs and of puppies) and especially by observation of the results of intracutaneous injection into the skin of the forearms of nursing children, she arrived at the conclusion that in certain cases *Staph. aureus* may be the sole pathogenic agent. Therefore, she considers the name impetigo contagiosa albostaphylogenes (Dohi) to be inappropriate and

proposes in its stead the name *impetigo albo-aureostaphylogenes* or *impetigo staphylogenes infantum*

Asano found the biologic behavior of the staphylococci of the normal flora of the skin to be identical with that of the staphylococcus causing impetigo. She believes that the reason that these organisms at times invade the subepidermal layers of the skin, producing the typical superficial vesicular lesion of impetigo, may be found in the difficulty in immediately getting rid of the sweat by evaporation. During the late part of the summer humid sultriness prevails in the region of the city of Osaka, where Osana is doing her work, and she believes that alkalimiza-tion (formation of ammonia) due to decomposition of the sweat and diminution of the sterilizing effect of drying are favorable to the growth of the staphylococcus. To these climatic factors are added the ease with which minute abrasions are produced in soggy, wet skin and the delicate make-up of the skin of nursing children.

Asano believes that the reason for the scarcity of this condition in nurslings before the fourth month of life lies in the fact that the sweat glands are not fully developed before that time.

J W BRENNAN, Chicago

A CASE OF ULCUS VULVAE ACUTUM WITH APHTHAE-LIKE LESIONS IN THE MUCOUS MEMBRANES OF THE MOUTH ASSOCIATED WITH ACUTE IRITIS M NISHIMURA, Lues Bull Soc japon de syph 12 149 (June) 1935

Nishimura reports the case of a 16 year old girl who suddenly became ill with chills, fever and general malaise. On the following day she complained of pruritus and a burning sensation of the vulva, three days later painful ulcerations developed on the labia minora pudendi, and the ulcers gradually became larger. One week later painful lesions developed on the mucous membranes of the mouth and throat.

On the inside of the left labium minus pudendi there was a large, oval, painful ulcer with a slightly undermined soft edge. The base was uneven and covered with a grayish-white purulent material. A similar lesion was seen on the inside of the right labium minus pudendi. Besides these two large lesions there were numerous small erosions on the inner side of the labia minora pudendi and in the vestibulum vaginae. The Wassermann reaction was negative, and bacteriologic examination revealed *Bacillus crassus*.

The pharynx was congested and the tonsils were swollen. The gums and the uvula showed aphthae-like erosions of irregular shape with sharp edges and erythematous areola. *B. crassus* was found in these ulcerations also.

Twenty-six days after the onset of the illness an acute iritis developed. The author expresses the belief that this case proves that *ulcus vulvae acutum* may spread by way of the blood stream and produce a general infection. Until 1927 eighteen cases of *ulcus vulvae acutum* were described in the Japanese literature.

BLOOM, New York

LIPOGRANULOMA AND ADIPONECROSIS SUBCUTANEA NEONATORUM G MOSBERG and E BEHR, Nederl tijdschr v geneesk 79 3050 (June 22) 1935

Mosberg and Behr observed a case of so-called adiponecrosis subcutanea neonatorum in a boy of 5 weeks. In connection with this case an investigation was made as to the pathogenesis of this disease and its possible connections with so-called lipogranulomatosis. The authors conclude that in the complex of etiologic factors that cause adiponecrosis subcutanea neonatorum an endogenous factor is the prime agent. Trauma has a certain importance as an exogenous cause, in this respect a relationship exists with lipogranulomatosis, in which, however, exogenous factors are predominant. As an important point of difference between these two diseases the chemical process is stressed, which in adiponecrosis subcutanea neonatorum is mainly a deposition of crystallized fats originating from the fatty tissue, whereas in lipogranuloma disintegration of fat occurs. These views could be confirmed experimentally.

VAN CREVELD, Amsterdam, Netherlands [AM J DIS CHILD]

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

FRANK C COMBES, M D , *Secretary*

Jan 7, 1936

MAX SCHEER, M D , *Chairman*

ROENTGEN RAY DERMATITIS TREATED WITH OINTMENT CONTAINING VIOSTEROL. Presented by DR BEATRICE KESTEN for DR ROBERT McLAUGHLIN

P. O , a man aged 29, born in Russia, is presented from the Vanderbilt Clinic. He was first seen in 1925. At that time he presented an occupational dermatitis venenata of one year's duration. From 1925 to 1927 he received forty one-fourth unit doses of roentgen radiation to the interdigital areas of each hand, with lead foil shielding. Roentgen rays were applied to the dorsum of the hand only. From 1928 or 1929 to 1931 he received twenty or more additional exposures to roentgen rays, but the hands were exposed from four angles so that the palmar, dorsal, medial and lateral aspects of the hands were exposed to the rays. After he had received fifteen doses in the second series of treatments, the patient noticed that red spots appeared on the skin, but the exposures were continued by the roentgenologist in charge. In 1931 the patient was treated for roentgen ray dermatitis by means of intensive ultraviolet irradiation given at weekly intervals and soaks of sodium thiosulfate applied twice a day. After three months his hands were worse, and he was hospitalized for a few months. At that time zinc oxide appeared to be the cause of his dermatitis venenata, and the acute condition of the hands was relieved by an ointment of lead oleate.

When he was discharged from the hospital the patient was given intravenous injections of liver extract experimentally. He received twenty of these in ten weeks, and much improvement in his general condition and some improvement in the condition of the hands resulted. After the injections were discontinued, his hands became worse again in spite of the fact that the liver therapy was continued orally and subcutaneously.

For the next year or so he was treated with viosterol orally and with boric acid ointment locally, but not much change resulted. In the spring of 1935 he was treated with an herb remedy without appreciable improvement.

In August 1935 treatment was started with an ointment containing about 8 per cent viosterol in a proprietary ointment base. The hands at that time showed a well developed telangiectasia complicated by keratoses, crusting, fissuring and, on the palms, vesiculation and exfoliation. The patient was able to close his hands about one-third but was unable fully to extend the fingers. After three days of the local treatment with viosterol the vesiculation and exfoliation of the palms began to regress, and within three weeks the crusting and vesiculation had disappeared. The patient was able to move his hands normally owing to the improved condition of the skin. At the present time it seems that the keratotic lesions have disappeared in spots and diminished in size in other areas. The patient states that the telangiectases are disappearing, and this is particularly noticeable on the right thumb. The left hand has been treated with the proprietary ointment base alone without viosterol for one week.

DISCUSSION

DR GEORGE C ANDREWS This patient received roentgen irradiation at the old Vanderbilt Clinic, later he went to a private physician, who gave him about fifty roentgen treatments. He came back to the Vanderbilt Clinic later, at which time he had a roentgen ray dermatitis. I think there is no doubt that there has been considerable improvement in the hands owing to the treatment with ointment containing viosterol. As far as I can remember, a year ago the hands were scaly and somewhat keratotic and fissured, and there was more or less stiffening of the joints as well as contracture and atrophy due to lack of use. I think that all these symptoms have improved considerably. The patient is able to move his fingers more freely.

DR HERMAN FEIT This case is of the utmost importance because up to now no treatment for roentgen ray dermatitis was known. A few years ago I presented a woman who had complete contracture of the hands together with the superficial changes characteristic of roentgen ray dermatitis. I treated her with viosterol and also with a high vitamin and salt-free diet. The beneficial result was apparent in this woman, she had not been able to close her hands for years, and after she had received the treatment she was able to open and close the hands. I was never able to explain how the salt-free and high vitamin diet could have such an effect. I should like to hear the opinion of Dr Blumenthal.

DR FRANZ BLUMENTHAL, Ann Arbor, Mich (by invitation) It is difficult to obtain any improvement in this condition, and the result in the patient presented is remarkable.

DR HERMAN SHARLIT I gather from the few remarks which have been made that something can be done for roentgen ray dermatitis. Apparently one may apply vitamins to the skin by means of salves. I should like to hear more about this. Is the treatment truly useful?

DR E WILLIAM ABRAMOWITZ The result obtained in this case is excellent. In carrying out the treatment, it would be wise to treat one hand with the proprietary ointment base alone without the viosterol to see the difference, if any is noticeable, in the results. I should also like to know if any of the members has had any experience with the use of the leaf of Aloe vera that has been reported to be efficacious in treating roentgen ray dermatitis (Collins, C E, and Collins, Creston. Roentgen Dermatitis Treated with Fresh Whole Leaf of Aloe Vera, *Ann J Roentgenol* 33 396 [March] 1935).

DR ADOLPH ROSTENBERG Is the leaf of Aloe vera incorporated in the ointment prepared by a manufacturing company in Buffalo? I had an experience with that salve recently. A patient had a radiation burn about the size of a 25 cent piece, it was not deep but was painful. After about three months of treatment with this ointment the ulcer closed up completely.

DR GEORGE C ANDREWS I think that Dr Rostenberg refers to an ointment made by Dr Creston Collins, of the Florida Medical Center, Venice, Fla. It contains extract of Aloe vera in 10, 20 or 40 per cent strength. I have used it and the leaves of Aloe vera extensively on patients with roentgen ray dermatitis and have seen some good results, although I think that in the majority of cases the benefits were no greater than those which would have been obtained by simple dressings moistened with saline solution. However, there is no doubt that the extract of Aloe vera possesses stimulating and healing properties affecting chronic ulcerative roentgen ray dermatitis, and some workers, who have used it more extensively than I, claim that even better results are obtained when the drug is used in early stages of the disorder.

I do not think that one should be too enthusiastic about the result in the patient presented tonight, because, although the hands are decidedly better, the same result might have been obtained by the use of many other preparations.

I have seen some cases of chronic roentgen ray dermatitis in which the telangiectasia tended to disappear after a number of years

DR MARION B SULZBERGER I agree with Dr Andrews that one must be cautious in ascribing too much credit to the therapy in this case, particularly as it is known that mild forms of roentgen ray dermatitis, and even some forms in which ulceration is present, show improvement as a result of mild topical remedies, such as, for example, boric acid ointment. Sometimes rapid improvement follows the use of petrolatum alone. One patient, a physician's secretary, with roentgen ray dermatitis of the hands, who had ulcers, keratoses, scaling and telangiectasia, was sent to me about three years ago. Rather haphazardly I gave ultraviolet irradiation to the hands. The patient was so much improved after the first few ultraviolet irradiations that I have continued to give such irradiation once or twice a week during the past three years. There has been marked improvement as a result of this treatment alone, topical applications have not been used. I thought it would be interesting to mention the beneficial effect of the ultraviolet irradiation on the roentgen ray dermatitis in my case, in view of the results with viosterol in Dr Kesten's patient. Perhaps there is a specific ultraviolet (photochemical) effect to be considered. I shall try to present my patient at a future meeting of the section.

DR ROBERT McLAUGHLIN (by invitation) Too much is not being claimed for the treatment used in this case. There are several obvious things to be considered. This man had an occupational dermatitis venenata that may have complicated the picture when this treatment was first started. The idea of using viosterol in the ointment was based on the beneficial effect of ultraviolet irradiation in the treatment of roentgen ray dermatitis obtained by others. In 1933 Drs Dokforsky and Platt used the same principle in the treatment of acne, but they gave viosterol internally. They thought that the benefits in acne were due to the effect of the viosterol on the skin. In roentgen ray dermatitis the oil glands are totally destroyed, and perhaps some of the effect from ultraviolet radiation has been the application of vitamins A and D to those areas. It is not known whether it is vitamin A or vitamin D that is doing the work, perhaps it is neither. All I can say is that the patient is much better. My co-workers and I will take photographs and follow this case. We hope to show that the telangiectasia is rapidly disappearing. The patient has been observed for results of this treatment for only about four months. The question of spontaneous healing was brought up. The last roentgen treatment was given four years ago, while the healing has occurred in four months. This patient had taken viosterol by mouth for one year. Dr Abramowitz asked about the advisability of using the proprietary ointment base alone on one hand and viosterol in the ointment on the other. That has been done in the past week only, and I believe that in the daylight a difference can be seen. I hope we shall have opportunity to present this patient again when there will be more conclusive evidence. I do not want to claim value for the treatment yet.

A CASE FOR DIAGNOSIS (LUPUS ERYTHEMATOSUS?) Presented by DR MAX SCHEER.

L M, a Negress aged 66, is presented because of a generalized eruption of two years' duration. The eruption is most marked on the face, thorax and extremities. It consists of numerous discrete and confluent areas of depigmentation, the largest measuring several inches in diameter. Some of the depigmented areas are covered with an adherent grayish scale. There is considerable scaling throughout the scalp, especially over the vertex. There is an associated moderate alopecia on the vertex of the scalp. The left ulnar nerve is slightly enlarged.

Examination for tinea on Dec 10, 1935, gave negative results. The results of the Wassermann test of the blood were negative, those of the Kahn test were plus-minus, those of the Kline diagnostic test, 2 plus, and those of the Kline exclusion test, 4 plus.

DISCUSSION

DR. ISADORE ROSEN I have seen a few similar disorders in Negroes, the early symptoms of which were those of a toxic erythema. After the condition had been present for some time the lesions acquired the clinical features of lupus erythematosus.

DR. HENRY D. NILES I agree with Dr. Rosen's diagnosis of disseminated lupus erythematosus. Depigmentation is quite common in Negroes with that condition. Dr. Scheer's patient also has lesions on the scalp which are not exactly similar, but which, I think, fit in with the picture.

DR. FRANK C. COMBES I agree entirely with what Dr. Rosen has said as to the difficulty of distinguishing between acute generalized disseminated lupus erythematosus and erythema multiforme. Sir Norman Walker, I believe, remarked that he knew of no way to differentiate between these two conditions clinically. The depigmentation, of course, is quite characteristic for Negroes. I know of no way to make a definite diagnosis of lupus erythematosus in this case, and the only means of arriving at a probable diagnosis is to study the configuration of the lesions.

DR. MAX SCHEER Of course, this patient was seen only a month ago, and hence the early manifestations of the disease were not observed. I know nothing about the lesions which appeared two years ago, and I cannot say whether they resembled erythema multiforme or not. Only the depigmentation, some atrophy and slightly scaling lesions remain. The only diagnosis one can now make tentatively from the lesions is that of lupus erythematosus. A biopsy was made today, and the results will be reported at the next meeting.

SARCOID Presented by DR. LEWIS B. ROBINSON

Z. H., a Negress aged 42, is presented from the Vanderbilt Clinic. She was previously presented in March and in May 1932. In 1926 she was found to have chronic pulmonary tuberculosis, and at that time she had a negative Wassermann reaction. In February 1932 she was admitted to the clinic with a generalized cutaneous eruption (the appearance is shown in photographs attached to the chart). The Wassermann reaction at that time was 4 plus, and the patient was presented as exhibiting tertiary syphilis. Treatment for syphilis was instituted, but no change occurred in the lesions. In April 1932 a biopsy was made, and the diagnosis was sarcoid. Until January 1933 the patient was treated with preparations of bismuth and of gold. She left the clinic at that time. When she returned in August 1933 she stated that her right foot had been swollen and that she had suffered from hoarseness for one month. All the cutaneous lesions had completely disappeared, their disappearance being coincident with the appearance of hoarseness and swelling of the foot. The reaction to old tuberculin was negative with a 1:10,000 dilution. The diagnosis of tuberculosis of the first metatarsal joint of the right foot and of tuberculous laryngitis was confirmed. In January 1934 a tuberculin test gave strongly positive results. Roentgenograms of the long bones showed no evidence of cyst formation. Those of the chest showed a diffuse peribronchial fibroid tuberculosis of about the same degree as that which was present in 1926.

SARCOID Presented by DR. LEWIS B. ROBINSON

E. E. S., a Negress aged 25, is presented from the Vanderbilt Clinic. The patient was presented in December 1932 (27:874 [May] 1933). At that time she had lesions on the face which had been present for three years. The reaction to tuberculin was negative. Histologic examination of one of the nodular lesions showed sarcoid of a small nodular type. The lesions at that time appeared to be similar to those which are present now. In May 1932 a roentgenogram of the chest was interpreted as showing evidence of soft extra densities scattered

throughout the pulmonary fields. This was considered consistent with advanced tuberculosis of recent origin. There was pleural thickening at the apex of the right lung. The costophrenic angles were clear.

The patient was treated with a gold preparation (4-amino-2-aurothiophenyl carbonic acid) for approximately a year without much improvement. She also received a salt-free diet for five or six months.

In November 1933 there developed what was probably a tuberculous bronchopneumonia or tuberculous pleurisy with effusion. In March 1934 the patient returned to the clinic, and it was found that all the cutaneous lesions had completely cleared up. Tuberculin tests showed the following results. With a 1:1,000 dilution the immediate reaction consisted of a 1 cm wheal and the delayed (forty-eight hour) reaction of a 1.5 cm swollen and red lesion. With a 1:10,000 dilution the immediate reaction consisted of a 0.7 cm wheal and the delayed (forty-eight hour) reaction of a 1.2 cm swollen and red lesion.

In November 1935 the patient again returned to the clinic, stating that there had been itching of the eyelids for two weeks previously and that this had been followed by a reappearance of all the cutaneous lesions, the manifestations being as at present.

DISCUSSION

DR. FRED WISE. I recall that Dr. Nomland described a series of disorders similar to that exhibited by this patient. He protested against the diagnosis of disseminated milium lupus and thought that the diagnosis of sarcoid was more correct. It is my opinion that in disorders like this certain lesions, like the one on the cheek which is discoid, are likely to show the histologic structure of sarcoid, whereas the ones situated around the eyelids, lips and mucocutaneous junctions are likely to resemble disseminated lupus miliaris. This is not surprising, especially in Negroes, in whom both types of histologic picture are frequently obtained when different lesions are examined at the same time. If the diagnosis of sarcoid was made in this case, it is probable that a discoid lesion was examined. I do not think it makes much difference what these individual lesions are called, as they represent different forms of tuberculosis with varying histologic structures.

DR. FRANZ BLUMENTHAL, Ann Arbor, Mich. (by invitation). This disorder represents a transition between lupus miliaris and the sarcoid forms, and it would be difficult to make an exact classification. All one can say is that there are a true hematogenous eruption and a high allergic state. In patients with these forms of tuberculosis the reaction to tuberculin may be strongly positive or negative (positive anergy). There has always been discussion as to whether it is necessary to distinguish all these forms of tuberculosis. My opinion is that there are advantages in distinguishing these variations of cutaneous tuberculosis because the clinical and microscopic pictures give the opportunity to draw important conclusions concerning the prognosis and the therapeutic procedure.

DR. T. J. RIORDAN. In a recent review of four cases of disorders of this type at the University Clinic the opinion just expressed by Dr. Wise was substantiated from a histologic standpoint. In other words, there were four cases in which the disorder was diagnosed clinically as milium lupus, but in two of these cases there was a question as to whether the clinical diagnosis should be sarcoid or milium lupus, the histologic picture confirming both diagnoses. Two sections from the same patient showed a tuberculous structure in one section and the tuberculoid structure of sarcoid in the other.

DR. EDWARD R. MALONEY. I agree with what Dr. Wise has said. I think one ought to be satisfied with calling this disorder tuberculosis cutis. So many Negro patients with tuberculosis of the skin exhibit different types of lesions—some having typical lesions of lupus miliaris and some sarcoid and sarcoid-like lesions—that I think one cannot apply a name that properly describes such a polymorphous eruption.

DR. MARION B. SULZBERGER I also agree with what Dr. Blumenthal has said and, as stated by Dr. Wise, in cases of these combined forms it is impossible to make one diagnosis which will embrace all the lesions. However, I agree with Dr. Blumenthal that in every case of tuberculoderma it is essential to try to make as exact a diagnosis of the type of tuberculosis as possible. I think that some of the lesions in this case are typical clinically of lupus miliaris faciei disseminatus. There are other lesions that resemble sarcoid, and still other lesions which somewhat resemble granuloma annulare. It is interesting that the tuberculoderms which this patient presents are of the anergic type. However, she reacted to tuberculin in a 1:1,000 dilution, I believe. This reaction is important, as Dr. Blumenthal said, as far as local resistance to the bacillus and general resistance are concerned. The point which, I think, one learns from disorders of this type is one I have learned only since I came to America, namely, as I have observed and frequently stated, there is a great deal of difference between tuberculosis of the skin in Negroes and that in the white persons. Such unusual combinations of tuberculoderms are much more rarely seen in white persons than in Negroes, and the reactions to tuberculin exhibited by Negroes are often atypical. Negroes generally show transitions from one anergic form to another and combinations of various forms, and they also frequently exhibit transitions between, and combinations of, the sarcoid and the lupus vulgaris types. In white persons such transitions and combinations are rarely seen. This is due, I think, to the well known variations in the racial allergic response to the tuberculous infection and to cutaneous infections in particular.

DR. B. LAPOWSKI Will Dr. Blumenthal explain in what manner the proper differentiation of tuberculous disorders of the skin, excluding lupus vulgaris, will help to select the correct treatment?

DR. FRANZ BLUMENTHAL, Ann Arbor, Mich. (by invitation) The hematogenous forms of high allergic states can be influenced by therapy much more easily than the localized forms of moderate allergic states like lupus vulgaris. In the first the general treatment with ultraviolet rays and the climatic and dietetic treatment used in the same way as in internal tuberculosis give much better results than in lupus vulgaris.

DR. EUGENE TRAUGOTT BERNSTEIN I wish to call attention to the work which was done by Herman Pinkus (*Arch f Dermat u Syph* 170:194 [May 31] 1934). He emphasized the complex multiplicity of various forms of atypical tuberculids occurring in one person. There also exists, in rare instances, a vicious circle between cutaneous lesions and pulmonary tuberculosis. In all probability the picture is similar to that observed in asthma and eczema: asthma disappears and eczema appears, or vice versa.

DR. SAMUEL M. PECK If evaluation of the tuberculin test is to be made it should be done properly. A single test is insufficient, and so is a single dilution. When one talks of several types of lesions of a tuberculous nature in the same patient and discusses the possibility of a transition from one type to another, one of course means that there has occurred in the allergy to tuberculin an actual change which accounts for such a transition. In order properly to study a case in which such a transition occurs, not only must the test be made with several dilutions of tuberculin but it must be made at several sites. It would be difficult for me to believe that a patient who is generally anergic would exhibit lupus vulgaris at one site and sarcoid at another if the hypersensitivity to tuberculin were the same all over the body. Another example can be observed by making repeated tests with the same dilution of tuberculin. At the time when the hematogenous tuberculous lesion resembles lupus vulgaris the reaction to tuberculin may be strongly positive. A short while after, when the sarcoid-like lesions develop, the reaction may be negative. What I wish to bring out is that when the reaction to tuberculin is properly evaluated the fluctuation and change in hypersensitivity to tuberculin can be detected. After all, that is the important information which the test gives.

DR FRED WISE There are certain points about which Dr Peck spoke which I should like to have cleared up I am almost certain that lupus miliaris disseminatus faciei, as originally described by Colcott Fox, is not the same disease as that which this patient exhibits tonight It is similar to it, but the distribution and the individual lesions are different This patient has lesions which are undoubtedly tuberculous The eruption is almost confined to the mucocutaneous junctions and is not disseminated over the cheeks as is the case in the disease described by Colcott Fox What is the reaction to tuberculin in the majority of cases of that disease, and how does it compare with the reactions in the disease exhibited by this patient, assuming that the two entities are clinically different? I wonder whether the reactions to tuberculin in this patient would be the same as they would be if the disease were lupus miliaris disseminatus faciei, regardless of the co-existence of lesions of sarcoid, which must change the reaction to tuberculin, as Dr Peck intimated I should like to have that point cleared up, if possible

DR. MARION B SULZBERGER Dr Peck will be able to answer Dr Wise's question It is inaccurate to call "lupus miliaris disseminatus" "lupus vulgaris disseminatus," for these two terms refer to what are certainly two entirely different and distinct forms of tuberculosis of the skin Dr Peck has compiled the largest statistics on the reaction to tuberculin in patients with lupus disseminatus miliaris faciei This condition is certainly anergic, as it can be classified in the so-called sarcoid group

DR SAMUEL M PECK I found that 50 per cent of a large group of patients with lupus miliaris disseminatus faciei exhibited negative reactions to tuberculin in a fairly high concentration This is a fairly high number of persons showing a negative reaction in association with a cutaneous lesion which is known to be of tuberculous origin and in which, in many cases, tubercle bacilli can be demonstrated This corroborates what Jadassohn first brought out, namely, that these patients tend to show an anergy to tuberculin The trouble with the statistics which I published was that in the published cases the reports were based on a single tuberculin test I am sure that if the tests had been made at different times the trend of the disorder would have been better evaluated In the cases which I reported the trend was toward a negative reaction The disorder exhibited by Dr Robinson's patient does not resemble lupus miliaris disseminatus faciei clinically

DR LEWIS B ROBINSON This patient was first presented with a diagnosis of lupus miliaris disseminatus faciei Subsequently a biopsy showed typical sarcoid She is presented because of her history during the last two years She responded to no therapy for a year After an attack of pleurisy with effusion, which was regarded as a tuberculous pleurisy, all the lesions immediately disappeared They did not reappear until a year later

I presented another patient with a similar disorder This second patient was presented before the section over three years ago, at which time she had multiple serpigmosus lesions thought to be due to syphilis because the Wassermann reaction was 4 plus That patient failed to show any response to active antisyphilitic treatment for a year The biopsy showed sarcoid There developed a tuberculous periostitis of a metatarsal bone of the foot and tuberculous laryngitis Within a month all lesions on the body disappeared That patient exhibited a negative reaction to tuberculin, but at the time she had a periosteal lesion the reaction became markedly positive It is of interest that both of these patients while they had sarcoid showed no signs of active tuberculosis However, as soon as the tuberculosis became active the sarcoids disappeared This, I believe, demonstrates that the sarcoid occurs during the anergic phase of tuberculosis and disappears when positive allergy to tuberculin is present

A CASE FOR DIAGNOSIS (PAPULONECROTIC TUBERCULID?) Presented by DR FRANK VERO

W J J, a Negro aged 35, born in the United States, is presented from the Vanderbilt Clinic because of an eruption of the skin and swelling of the right side of the neck of four months' duration. The swelling in the neck developed suddenly, and the cutaneous eruption appeared shortly afterward.

There are numerous brownish-reddish papules, from the size of a pinhead to that of a pea, some show slight scaling, others show small necrotic areas in the center. There is a marked cervical adenitis on the right side.

The Wassermann reaction of the blood was negative. Roentgenograms of the chest showed no abnormalities. A biopsy was reported on by Dr Gerald F Machacek as follows: Histologically the disorder is either a papulonecrotic tuberculid or a tertiary syphilitic ulceration. The ultimate diagnosis depends on clinical evidence.

DISCUSSION

DR CHARLES WOLF This case is rather interesting in view of the fact that the Wassermann reaction is negative and that the patient has two pathognomonic signs of late syphilis. He has leukoderma colli and a gummatous infiltration of the right sternocleidomastoid region. These two manifestations are rather resistant to early improvement under antisyphilitic treatment. The other lesions, I think, are not tuberculids but are probably papular urticarial lesions.

DR ISADORE ROSEN Another diagnosis that should be considered is that of Hodgkin's disease. It is unusual to see such a widespread dissemination of lesions associated with papulonecrotic tuberculids. Another unusual feature is the enlargement of the glands in the neck. This manifestation of tuberculosis is usually found much earlier in life. I therefore suggest that roentgenograms of the chest be made for evidence of mediastinal glandular enlargement and that further studies be made to rule out a disease of the hematopoietic system.

DR FRANK VERO This patient was originally referred to the surgical department of the Presbyterian Hospital for diagnosis of the condition of his neck. The disorder was thoroughly studied in both the medical and the surgical departments, where several diagnoses have been considered: first a diagnosis of actinomycosis, then one of abscess of the neck, and finally one of lymphadenitis tuberculosa. Syphilis has not been considered, and the patient has received no antisyphilitic treatment. Wassermann tests have all given negative results. The diagnosis of Hodgkin's disease was not considered. Repeated blood counts have given negative results except for the fact that the hemoglobin content was 68 per cent. The patient was referred to the dermatologic department on account of an eruption involving the neck, both axillae and the lower portions of the legs. The eruption on the neck was follicular and pustular, and I first made a diagnosis of folliculitis due to some pyogenic organism. The eruption in the axillae and on the legs appeared entirely different from that on the neck. The lesions were papular, raised and reddish brown, some had necrotic centers, resolving gradually and leaving pitted scars as seen in typical papulonecrotic tuberculids. A biopsy was made from a lesion on the leg, and Dr Machacek considered the disorder to be papulonecrotic tuberculid or possibly tertiary syphilis. The patient had recently received two roentgen treatments to the neck, the last one, I think, was given two days ago. The gland on the neck has enlarged considerably since.

SYMMETRICAL ANOMALY OF THE NAILS Presented by DR PAUL GROSS

A B, a woman aged 26, is presented from the Hospital for Joint Diseases. The patient remembers having had the condition of the nails for at least ten years and dryness of the skin for about six years. Her father is a physician and has a similar condition of the nails of both thumbs and forefingers. Four brothers and two sisters show no abnormalities in the nails.

The nails of both thumbs show deep transverse grooves and grayish transverse superficial fissures. These changes are confined to the middle portions of the nails throughout their entire length, giving a streaklike appearance. The skin of the corresponding basal portions of the nails appears hyperkeratotic. There are slight furrows in the central portions of the nails of both index fingers. The palms show coarseness of the skin and increased markings, a feature unusual for the hands of a person doing only a small amount of housework and no laundry work. There are a follicular keratosis of the legs and ichthyosis-like scaling on the knees and elbows. The condition of the skin and of the palms is suggestive of ichthyosis.

ACTINOMYCOSIS OF THE JAW (CURED) Presented by DR BEATRICE KESTEN

M. H., a Negress aged 37, is presented from the Vanderbilt Clinic. She was presented on Jan 2, 1935 (ARCH DERMAT & SYPH 32:503 [Sept] 1935). She had been admitted to the Presbyterian Hospital on Dec 4, 1934, because of swelling of the left side of the face of eight weeks' duration. The swelling had occurred after extraction of a tooth. The patient then presented the typical suppurating lumpy jaw with involvement of the mandible and skin of the entire left cheek and upper part of the neck seen in actinomycosis. She was unable to open her mouth more than 1 cm. Actinomyces was found in the pus and grown in culture.

The patient was given 25 drops of saturated solution of potassium iodide but an intolerance soon developed. She then received 150 roentgens (160 kilovolts) of radiation filtered with 1 mm of aluminum at a distance of 25 cm, six treatments being given at weekly intervals and inhalations of ethyl iodide for three weeks, totaling 30 cc. Four infected teeth were removed, and fluctuating abscesses were incised.

The patient received no treatment for six months and has remained well. Culture of material from the tonsils for Actinomyces on Nov 22, 1935, gave negative results.

NEW YORK DERMATOLOGICAL SOCIETY

EUGENE F. TRAUB, M.D., *Secretary*

Jan 28, 1936

RAY H. RULISON, M.D., *President*

DERMATITIS HERPETIFORMIS (DUHRING) Presented by DR J. FRANK FRASER

J. R., an American boy aged 8 years, was first seen on May 20, 1935, exhibiting a generalized eruption which had been present for one year. It began on the legs and back and has spread to the chest, neck and face. The lips are also involved. The initial lesions were small vesicles. There is intense pruritus.

Urinalysis gave negative results. The blood cell count showed 4,400,000 red cells, 18,800 white cells and 70 per cent hemoglobin. The differential count showed 68 per cent polymorphonuclear leukocytes, 21 per cent lymphocytes, 7 per cent mononuclear leukocytes, 4 per cent eosinophils and no basophils. The red cells showed a slight decrease in size. A smear from a vesicle showed 12 polymorphonuclear leukocytes to 1 eosinophil. Allergy tests with potassium iodide in 25 and 50 per cent solutions gave negative results. Determination of the basal metabolic rate was ordered, but the internist considered it inadvisable to make the test at this time. Biopsy of a vesicular lesion on the shoulder was reported to show Dühring's disease.

Treatment has consisted of soothing lotions, packs of weak solution of potassium permanganate and roentgen radiation. On Dec 31, 1935, the patient received

one-quarter skin unit of unfiltered radiation to the chest, back, neck, lips and upper portion of the arms. On Jan 7 and 16, 1936, he received another one-quarter skin unit of radiation to the affected areas. Some improvement has resulted from roentgen therapy.

DISCUSSION

DR HENRY H WHITEHOUSE. I think that the diagnosis of dermatitis herpetiformis is the most logical one. Eruptions in the mouth and on the lips are rather unusual, but the itching, the grouping and the recurring attacks indicate that the disorder is Duhring's disease rather than pemphigus. A number of teeth have been removed, but I understand that the eruption appeared before the teeth were extracted. In consideration of the itching, the distribution and the grouping, I agree with the diagnosis.

DR A BENSON CANNON. I agree with the opinion expressed by Dr Whitehouse, although I am more in favor of the diagnosis of erythema multiforme because of the location of the eruption, the edematous character of the lesions, the involvement of the mucous membranes of the lips, the absence of itching and the youth of the patient. I suggest that the patient be given liver orally and injections of liver extract every other day or even daily. Dr Rhodes, of the Rockefeller Institute, expressed the belief that in many cases these bullous lesions of the mucous membranes are due to a vitamin deficiency, and he has obtained splendid results in some cases by giving large amounts of liver extract.

DR HOWARD FOX. In my opinion this patient presents the classic signs and symptoms of Duhring's disease, namely polymorphism, grouping, itching and a tendency to relapse. The presence of oral lesions does not exclude Duhring's disease, though it must be admitted that oral bullae are much less common in that disorder than in pemphigus. I do not think that a diagnosis of pemphigus should be considered as there are no bullae on the cutaneous surface.

(Dr Fred Wise, Dr Edward R Maloney, Dr Frank Combes and Dr Eugene F Traub agreed with the diagnosis of Duhring's disease.)

A CASE FOR DIAGNOSIS (ROSACEA-LIKE TUBERCULID? ROSACEA? LUPUS ERYTHEMATOSUS?) Presented by DR EUGENE F TRAUB

Mrs M M, a housewife aged 28, born in the United States, complains of an eruption on the face which first appeared in June 1935. She states positively that she did not suffer an acute sunburn, but she believes that the heat or possibly slight exposure to the sun's rays may have been a factor in causing the disorder. Two other factors which the patient thinks may have been precipitating causes were the sudden and accidental death of her husband and the death of her baby which occurred directly after delivery. These events have made her exceedingly nervous, and in view of the fact that one of the diagnoses first considered was that of rosacea, these events may actually have played a part in the etiology.

The lesions are arranged somewhat in a butterfly fashion on the cheeks and nose. The individual lesions, however, do not suggest lupus erythematosus. They are difficult to describe because it is hard to determine their exact type. At times they seem to be pure papules or tiny nodules, while at other times they appear to be slightly pustular. In the two or three weeks that the patient was under observation there was little response to treatment. There is no history of ingestion of drugs. Tests with tuberculin in graded dilutions gave moderately positive results in the more concentrated dilutions.

DISCUSSION

DR HOWARD FOX. The clinical diagnosis in this case is, I think, extremely difficult. The disorder does not have the appearance of ordinary rosacea, and there is no history of gastro-intestinal disturbance, which is so common in that disease. The diagnosis seems to lie between lupus erythematosus and some form of tuberculosis.

DR JOSEPH J ELLER I am more inclined to regard the condition as lupus vulgaris than as lupus erythematosus

DR J FRANK FRASER The diagnosis lies between lupus erythematosus and true tuberculosis

DR A BENSON CANNON I favor the diagnosis of tuberculosis The yellow color of the nodules and the crusting are more suggestive of lupus vulgaris than of lupus erythematosus

DR EDWARD R MALONEY I cannot make a diagnosis in this case The disorder is either lupus erythematosus or tuberculosis.

DR HENRY H WHITEHOUSE I think it is difficult to diagnose this disorder on the basis of the clinical observations, and the location of the lesions makes it rather hard to obtain material for a biopsy Clinically I cannot distinguish the condition from lupus erythematosus If material for a biopsy can be obtained, microscopic studies might be helpful

DR EUGENE F TRAUB My first idea was that the disorder was plain rosacea In view of certain features, and particularly because of the associated seborrhea, I gave the patient one or two doses of the roentgen rays of one-quarter skin unit each It is my opinion that the eruption as seen today is worse than it was before While I know that rosacea does not always respond favorably to roentgen therapy, I do not believe that the flare-ups are usually as pronounced as is the case in rosacea-like tuberculid In all cases of this type which I have seen the disorder has always been much aggravated after treatment with the roentgen rays For this reason the diagnosis that I now favor is that of rosacea-like tuberculid

ACRODERMATITIS CONTINUA (HALLOPEAU) Presented by DR A BENSON CANNON

S. N., a man aged 25, is presented from the New York City Hospital He sustained an injury to the right index finger at the age of 2 years, which resulted in loss of the nail Since the onset of the condition all the other fingers, the palmar and dorsal surfaces of both hands and the nails and plantar surface of the left foot have gradually become involved There is a definite history of trauma accompanying each new spread of the disease The patient had received little treatment until eight years ago, when he was given a series of eight roentgen treatments over a period of two years without benefit He was then given a course of eight injections of arsphenamine, eight injections of a bismuth preparation and three injections of mercury as a therapeutic test, although the Wassermann reaction of the blood was negative at that time These injections caused all the lesions to clear, but the nails showed no improvement, and since that time the condition has gradually returned On several occasions the patient had been told that his only hope for a cure was to have all the infected fingers amputated

There are lesions on the first and second fingers of the right hand, on the second, third and fourth fingers of the left hand, on the dorsal and palmar surfaces of both hands up to the wrist joint and on the third, fourth and fifth toes, interspaces and anterior half of the plantar surface of the left foot The lesions are definitely demarcated, having a raised overhanging border, beyond which the skin is normal They are covered with thick, brown scales, the peeling off of which reveals a smooth, red base in which there are numerous pinhead-sized white pustules The nails are for the most part absent, only rudiments of the nail keratin remaining on several of the affected fingers and toes The nail beds are covered with scales Under the scales the base is smooth and contains white pustules like those which are present on the palm and back of the hand

The Wassermann reaction of the blood was negative Chemical examination of the blood, urinalysis and determination of the arsenic content of the urine gave negative results Culture from the margin of the lesion showed *Staphylococcus albus* Blood serum gave a negative agglutination reaction for this organism Roentgenograms of the hands and feet showed small bony spicules coming off

the base of the terminal phalanges of the involved digits. Roentgen examination of the heart, lungs, gastro-intestinal tract and gallbladder showed no abnormalities.

Generalized ultraviolet irradiation and local irradiation to the hands and feet were given twice a week. Autogenous vaccine was given twice a week in gradually increasing doses. Typhoid vaccine was given once a week for six weeks, the therapy caused the temperature to rise to 103.4 F for from eight to ten hours. The patient was given colloidal manganese once each week. After the administration of typhoid vaccine was discontinued 5 cc of sterile cow's milk was injected once a week, this caused the temperature to rise to an average of 102 F for five or six hours on each occasion. The hands and feet were soaked in solution of potassium permanganate twice each day for an hour. Each night for the first two weeks a 10 per cent solution of salicylic acid in olive oil was applied. Twice each week the scales were removed and all visible pustules were opened. The patient has received a high vitamin, high caloric diet.

Steady improvement was noted from the day the treatment was begun, this was particularly evident after each paroxysm of fever. The number of pustules became less numerous each week, the scales became less prominent, and finally normal epithelium appeared in islands throughout the involved area, in time it joined to cover all the previously involved areas, the nail beds being the last to recover.

The patient is presented to show the excellent therapeutic results.

DISCUSSION

DR EUGENE F. TRAUB. I have been much interested in this patient for many years, and I wish to congratulate Dr. Cannon on the excellent result he has obtained. Certainly at no time since the onset of the disease has this young man's skin been in as good condition as it is today. He was in the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital for months, and although some improvement always resulted from treatment a cure was never approached, and in fact I had almost come to believe that the condition was incurable. The patient should be grateful for the result achieved.

A CASE FOR DIAGNOSIS (DERMATOPHYTOSIS WITH DERMATOPHYTID? SCLERODERMA?) Presented by DR. EUGENE F. TRAUB

R. S., a woman aged 46, born in Russia, was first seen on Jan. 6, 1936, presenting an eruption of four months' duration on the inner aspect of the lower portion of the right leg. The surface was slightly erythematous, and there was a deep, almost boardlike mass in the subcutaneous tissue. The skin covering the involved area could be wrinkled and did not seem to be particularly hidebound.

The Wassermann and Kahn tests and urinalysis gave negative results. The results of mycologic examinations were as follows. The reaction to trichophyton was 4 plus, that to oidiomycin was 3 plus on the patient's arms. A positive wheal reaction appeared about twenty minutes later on the affected leg, and at the site of injection a nodular mass appeared, which remained for at least five or six days. Examinations for tinea gave the following results. Smears from the first, third and fourth interdigital spaces of the right hand and the first and third interdigital spaces of the left hand were all negative, those from the fourth and fifth toe-nails of both feet were positive for mycelia, those of the fifth toe-nail of the right foot were suspicious, and those of the fourth toe-nail of the right foot were negative.

The biopsy report was as follows. The microscopic diagnosis was scleroderma. Aside from a moderate telangiectasia throughout the cutis there was little of importance to be seen. The epidermis showed little change, the basal cell margin was intact, and the granular layer was present throughout. Throughout the subcutaneous tissue were numerous coil glands, several of which were tremendously dilated. The vessels in the fat region were somewhat thickened, and there was marked irritation of the fat. The elastic tissue was intact.

DISCUSSION

DR JOSEPH J ELLER I do not think that the disorder is scleroderma. It might fit into the clinical description of *periphlebitis nodularis necroticans*.

DR J FRANK FRASER I cannot make a diagnosis.

DR HOWARD FOX As the histologic examination shows no evidence of scleroderma, that diagnosis must be excluded. One should consider the possibility of an erythema nodosum-like eruption due to fungous infection.

DR EDWARD R MALONEY I do not believe that the disorder is scleroderma or erythema nodosum. It may be due to some low grade infection which has become manifest as a localized lymphangitis.

DR FRANK C COMBES I do not see how any one can be expected to make a diagnosis in this case on the basis of the presentation. I understand that the lesions are noninflammatory. The picture at present does not suggest scleroderma. There is marked inflammation, probably as a result of the removal of a section of skin for histologic examination. There does not seem to be any evidence of hidebound skin over the involved area.

DR HENRY H WHITEHOUSE I cannot make a diagnosis.

DR EUGENE F TRAUB An examination of the section of skin removed from the center of this lesion seemed to rule out the diagnosis of scleroderma. Whether the disorder can be termed an "id" or not, I am not prepared to say positively. It may be merely a peculiar type of lymph stasis, but as other cases of lymph stasis have been observed in which tinea apparently played a definite rôle, it may be a factor in this case as well. Trichophytin injected into an unaffected portion of the skin of the leg produced a lesion somewhat similar to the one now present. In cases in which there was a positive reaction for tinea associated with an "id", the latter has always cleared up coincidentally with the clearing up of focal infection of the feet with tinea. The treatment of tinea has been deferred so that the eruption would not be altered before the patient was presented. I shall report at a later meeting whether or not the lesion on the leg has responded to this type of therapy.

PARAPSORIASIS VARIOLIFORMIS Presented by DR FRED WISE

E S, a woman aged 41, was presented before the Section of Dermatology and Syphilology of the New York Academy of Medicine in October 1934. She is presented again because of the interest attaching to a recurrence of the varioliform type of parapsoriasis, associated with lesions of the usual form of pityriasis lichenoides chronica. The eruption disappeared during the summer of 1935, when the patient was exposed to the sun's rays on the beach, it recurred at the end of the summer. The eruption exhibited tonight is of several months' duration.

Brownish red lenticular spots are disseminated over the trunk and limbs, they are slightly infiltrated and covered with a dry adherent scale. Besides these typical lesions there are also a few frankly vesicular lesions and several small superficial ulcers, the sites of previous vesicular lesions.

The Wassermann and the Kahn test were negative. The histologic examination showed parapsoriasis.

DISCUSSION

DR HENRY H WHITEHOUSE The diagnosis of parapsoriasis varioliformis is the best diagnosis I can make on the basis of the clinical appearance.

DR EUGENE F TRAUB I agree with the diagnosis as presented, this patient shows practically all the various types of lesions characteristic of this condition. The disorder apparently responds to ultraviolet irradiation or exposure to the sun's rays, or the remissions that are observed from time to time may be spontaneous and occur in the usual course of the disease.

DR FRANK C COMBES I agree with Dr Traub.

DR A BENSON CANNON The disorder is interesting, and the lesions are so strikingly similar to those found in psoriasis that I should think it would be interesting to follow the patient, if possible, over a period of several years in order to see whether psoriasis does not develop. The stippling of the nails is also suggestive of psoriasis.

DR FRED WISE When this patient was first presented, practically all the lesions were vesicular. Now she presents lesions of scaling parapsoriasis together with vesicular lesions.

SCLERODERMA Presented by DR. EUGENE F. TRAUB

E. D., a man aged 52, born in the United States, was first seen on Jan. 22, 1936. The patient states that he had never had any cutaneous trouble until October 1931. At that time he first noticed thickening of the skin on the left side of the abdomen. Later he began having pains in all the joints of both lower extremities. This was diagnosed as arthritis and has been followed by some deformity of the toes and stiffness of the feet, so that walking became difficult. About three years ago the patient began to notice increasing areas of thickening of the skin, these appeared first on the shoulders and within six months involved the chest, abdomen, legs, thighs and arms.

On the anterior aspect of the chest and abdomen, on the arms as far as the elbows, on the legs up to the knees, on the anterior aspect of the thighs, on the hands and feet and on the back are areas of erythematous woody deep-seated lesions with slight scaling. On the hands and feet are areas of secondary infection. The fingers show little movement and are rigidly flexed.

Chemical examination of the blood on Jan. 20, 1936, showed 113 mg. of sugar and 28 mg. of urea nitrogen per hundred cubic centimeters. The Wassermann reaction has been repeatedly negative. Roentgenograms of the skull, pituitary gland, adrenal glands and chest showed no abnormalities. Those of the bones showed trophic changes and atrophy due to disuse. There is a history of ingestion of arsenic, and arsenic was found in the urine.

The patient has been treated by Dr. Rubin with thyroid, potassium permanganate and salves.

DISCUSSION

DR HENRY H. WHITEHOUSE The condition of the hands is an unusual feature, but of course the disorder is scleroderma.

DR A. BENSON CANNON I have been much interested in the work that has been done by physicians working at the Cornell Medical Center in removing the parathyroid glands in cases of scleroderma. They report that excellent results follow removal of a portion of the parathyroid tissue. They have also obtained splendid improvement in cases of scleroderma by giving injections of calcium. I suggest that the patient be put in proper physical condition for operation, the secondary infection of the hands be cleared up and then a parathyroidectomy be performed. Certainly, his pitiful state calls for radical treatment.

DR J. FRANK FRASER I have observed only one case in which a parathyroidectomy was performed. There was no improvement in the condition when the patient was discharged from the hospital.

A CASE FOR DIAGNOSIS (*MYCOSIS FUNGOIDES Homine Rouge?*) Presented by DR. FRED WISE

H. H., a man aged 53, states that the onset of his disease occurred in March 1935 in the form of diffuse redness and itching of the hands and forearms. This attack cleared up after topical remedies were applied, but the disorder recurred with increased intensity in October 1935. The redness and itching then rapidly spread up the arms and gradually involved the skin of the entire body and of the face.

There is a uniform diffuse dusky red eruption affecting all parts of the body but somewhat less marked on the chest than elsewhere. The skin is smooth and

noninfiltrated on the trunk and face, but the hands and forearms present a moderate grade of thickening and hyperkeratosis, while the palms and soles are definitely hyperkeratotic. The skin of the face is almost purplish red, resembling extremely weather-beaten skin. There are no marks of scratching, but the patient complains of moderate itching, especially at night.

The histologic picture is that of an early stage of mycosis fungoides.

NOTE.—Subsequent examination, on June 3, 1936, revealed innumerable nodular infiltrations from the size of a pea to that of a hazelnut scattered all over the torso and presenting the typical appearance of granuloma fungoides.

DISCUSSION

DR HENRY H WHITEHOUSE I agree with the diagnosis of mycosis fungoides.

DR EUGENE F TRAUB This is the first time that I have seen mycosis fungoides begin in this manner. Though cases in which such an onset occurred have been recorded, they appear to be exceedingly rare in this country. The only lesion that I observed on the patient which would have suggested mycosis fungoides to me is a plaque in the left axilla which definitely shows a certain amount of infiltration and a suggestion of a horseshoe configuration.

DR FRANK C COMBES I agree with the diagnosis as presented. An interesting point is the pallor in the axillae and about the nipples. Such pallor is of frequent occurrence in cases of erythroderma. I have never come to any conclusion as to its significance.

DR J FRANK FRASER This is the *homme rouge* type of mycosis fungoides, and the clinical diagnosis can frequently be confirmed by microscopic examination.

DR A BENSON CANNON I could not make a diagnosis of mycosis fungoides in this case, and I doubt that that disease is present even though the histologic picture indicates it. All I could possibly see was that the patient had a generalized dermatitis. I think that the patient should be thoroughly studied in regard to metallic poisoning or contact dermatitis.

DR. FRED WISE In view of the histologic report by Drs. Satenstein and Sachs it is probable that the eruption is an example of the *homme rouge* type of mycosis fungoides described by French authors.

ALOPECIA TOTALIS, MILIA OF THE EYELIDS Presented by DR FRED WISE

A T, a man aged 21, born in the United States, states that he has suffered from loss of hair since the age of 2½ years. The disease began as a patchy alopecia of the scalp associated with loss of eyebrows and eyelashes following an attack of measles at the age of 2½ years. The disease progressed steadily, and complete loss of mature and lanugo hair occurred six months ago. Milia of the upper eyelids also appeared after the attack of measles in infancy.

Roentgenograms of the skull revealed a normal pituitary gland. The basal metabolic rate, the arsenic content of the urine and the dextrose tolerance were all normal. The Wassermann and the Kahn test were negative.

The patient exhibits obvious symptoms of endocrine imbalance, the most evident being excessive obesity and an extension of the skin of the scrotum to form a hood-shaped arch over the root of the penis on its dorsal aspect. The testes appear to be normal but are retracted upward toward the inguinal ring.

DISCUSSION

DR. HOWARD FOX In my opinion further treatment with anterior pituitary extract (antutrin) is inadvisable. Like many other physicians, I have given this remedy a reasonably thorough trial in cases of alopecia areata and have never seen the slightest benefit result from its use. I have heard expressions of similar opinion from colleagues in different parts of the country. I think it is important that the negative results obtained by the members of this society be put on record in order to prevent further waste of time and money on the part of patients.

DR J FRANK FRASER I suggest that a spectroscopic analysis be made to determine the presence of metals

DR JOSEPH J ELLER I agree with Dr Fox that the therapy with anterior pituitary extract (antuitrin) has not proved to be what it was claimed I have tried it and have obtained no results so far This patient's basal metabolic rate is reported to be normal, but clinically there is a definite dysfunction of the pituitary gland and possibly of the thyroid gland Regardless of the basal metabolic rate, my advice is to give this patient pituitary and thyroid extracts

DR EDWARD R MALONEY I do not think that the aforementioned gonadotropic hormone is of any value in this type of disorder

NAEVUS PIGMENTOSUS (MELANOMA) Presented by DR J FRANK FRASER

H G, a youth aged 17, was previously presented before the Manhattan Dermatologic Society

The patient is presented for suggestions as to therapy

DISCUSSION

DR EUGENE F TRAUB I believe it can be stated without a doubt that the lesion is a nevus, but whether it is an ordinary pigmented nevus or a blue nevus I find it difficult to say after a mere inspection At present the growth certainly seems to be benign, but because it is located where it is more or less constantly subjected to pressure and possible trauma, I believe it is most advisable to remove it in the hope of preventing a future malignant change

DR HENRY H WHITEHOUSE I cannot say whether the nevus is benign or malignant I should hesitate to remove it surgically

DR HOWARD FOX I believe that the lesion is a benign melanoma My advice would be to excise it as it is subject to constant trauma

DR JOSEPH J ELLER I was under the impression that a blue nevus was level with the skin The only way to make a final diagnosis is by microscopic examination I should not treat the nevus as a benign lesion

DR A BENSON CANNON While I believe that the lesion is a benign blue nevus, I should like to call attention to the possibility of its being an angioma I have records of two cases in which competent physicians had made a diagnosis of melanoma and in which on removal the growth was found to be an angioma I do not believe that I have ever seen a soft fluctuating tumor in the center of a pigmented nevus such as this patient presents

DR EUGENE F TRAUB I have carefully read the description of what a blue nevus should look like Unfortunately the color is not necessarily a deep blue, but according to Tieche, depending on the depth of the lesion, on the natural color of the patient's skin, on the location and probably on other factors, the color may even be a brownish or blackish blue For this reason I do not see how it is possible on clinical inspection to distinguish a blue nevus from an ordinary slate-black mole As the cells of the blue nevus are similar to those constituting a mongolian pigmented spot, I believe that blue nevi become malignant less frequently than other types of pigmented nevi When one does become malignant it is supposed to develop into a melanosarcoma, in contradistinction to the ordinary pigmented nevus which becomes a melanocarcinoma In this case I do not believe that the lesion is a vascular nevus of any type, although, I repeat that it is impossible to determine this with certainty on clinical grounds alone In this location and because of the pressure to which the lesion is subjected I can easily conceive that a vascular lesion might take on the appearance of the present one

DR EDWARD R MALONEY I should say that this condition is a benign melanoma The elevated part of the lesion may suggest angioma, but certainly the border is a pigmented lesion

DR FRED WISE I agree with the diagnosis of benign melanoma. Because of its location, I believe it is best to remove the lesion, as there is a possibility of its becoming traumatized. I should remove it by wide and deep excision.

DR J FRANK FRASER I have nothing to add. I am thankful for suggestions as to treatment.

ACNE VARIOLIFORMIS Presented by DR EUGENE F TRAUB

G W, a man aged 36, born in the United States, had a typical papulonecrotic eruption for from ten to fifteen years, at times the condition practically cleared up. The lesions appear in crops, being scattered over various areas of the face and scalp and being particularly noticeable about the margins of the hair and the nose. The chief reason for presenting the patient is that the resultant scars are much larger than those usually seen in this disease, some of them measuring from 5 to 6 mm in diameter and having a depth of from 1 to 2 mm. Such large scars appear to indicate that the active lesions have also been unusually large, and this seems definitely to be the case.

Tuberculin tests gave negative results with 1 1,000,000 and 1 100,000 dilutions and a plus-minus reaction with a 1 10,000 dilution. The condition was made worse by treatment with tuberculin. The biopsy showed a low grade pustule and changes not incompatible with the diagnosis of acne varioliformis.

DISCUSSION

DR A BENSON CANNON While I believe that the condition is suggestive of acne varioliformis I have never seen such terrific scarring and such large and crater-like scars as this patient presents, especially over the nose, to result from acne varioliformis. There are no active lesions that are suggestive of that disease. The few early lesions that the patient has are nothing more than blood-crusted edematous papules. Unless the condition has been thoroughly investigated, I should suggest that this patient be observed with a view to the possibility of the condition's being self-inflicted.

DR EUGENE F TRAUB I admit that I did not consider the diagnosis of neurotic excoriations in this case, and therefore the patient was not particularly studied with this thought in mind. However, I have known the patient for a number of years and at no time has he impressed me as a neurotic person. The lesions are too uniform, and the pitting is of the type seen only after smallpox, chickenpox, acne varioliformis, papulonecrotic tuberculid or similar disease in which all lesions result in deep pits of practically uniform size. The reason I presented the patient was because I thought that the disorder was exceedingly typical, the only unusual feature being the large size of the lesions and the scars resulting therefrom.

REPORT ON A CASE PREVIOUSLY PRESENTED DR EUGENE F TRAUB

L C, a woman aged 26, was presented for diagnosis before this society on Dec 17, 1935 (ARCH DERMAT & SYPH 34: 534 [Sept] 1936). The eruption was present on both legs. *Endamoeba histolytica* was found in the stools. An examination of the urine revealed 33 mg of sodium bromide per hundred cubic centimeters. No iodides were found. When examinations were made in the Massachusetts General Hospital the results of examinations for bromide and iodide content of the urine were said to be negative. In view of the fact that in the discussion one or two of the members mentioned the possibility of an eruption due to a drug I think that this finding is of importance.

REPORT ON A CASE PREVIOUSLY PRESENTED DR EUGENE F TRAUB

A O, a man aged 35, was presented before this society on Nov. 26, 1935 (ARCH DERMAT & SYPH 34: 525 [Sept] 1936), with a diagnosis of papulonecrotic tuberculid and granuloma annulare.

I wish to recall this patient's condition to the minds of the members. The condition was diagnosed as an extensive granuloma annulare involving the arms.

and shoulders, a few scattered lesions being also present on the thighs and on the trunk. The patient also had an eruption which was thought to be a papulo-necrotic tuberculid, but this may have been an error, as the latter lesions seemed to undergo spontaneous involution with scarring while the patient was under observation. The patient was given one dose of seven-eighths skin unit of filtered roentgen rays to the granuloma annulare lesions. These have all disappeared, apparently as a result of this treatment.

MINNESOTA DERMATOLOGICAL SOCIETY

F W LYNCH, *Secretary*

Feb 7, 1936

L H WINER, M D, *President, Presiding*

LICHEN PLANUS OF THE EYELIDS Presented by DR H E MICHELSON, Minneapolis

A woman aged 29 is presented because of a retiform melanosis confined to the eyelids. The rest of the skin and the mucous membrane are not involved. The biopsy specimen showed changes characteristic of lichen planus. Four roentgen treatments have been administered, and considerable improvement has resulted.

DISCUSSION

DR HAMILTON MONTGOMERY, Rochester Dr Michelson's case is a duplicate of one presented in Chicago, in which he also made the diagnosis of lichen planus of the eyelids.

LYMPHOGRANULOMA VENEREUM Presented by DR JOHN F MADDEN, St Paul

M C, a Negro laborer aged 45, noticed a bilateral painful inguinal adenitis about five weeks ago. The nodes became matted and grew progressively larger and more painful. The patient had sexual intercourse with a Negro prostitute in the latter part of November 1935. No penile lesion was noted. The nodes in each inguinal region are the size of a fist and contain a large amount of pus. The patient complains of constipation and extreme pain on defecation, but proctoscopic examination gave negative results. Ducrey bacilli were not found in the pus, Frei tests and Wassermann examinations of the blood gave repeatedly negative results.

A CASE FOR DIAGNOSIS (LYMPHOGRANULOMA VENEREUM?), PENILE CHANCRE, MACULAR ERUPTION OF SECONDARY SYPHILIS Presented by DR JOHN F MADDEN, St Paul

E J, a laborer aged 35, was first seen on Jan 10, 1936, presenting a superficial ulcer at the urethral meatus which was indurated and exuded serum. The ulcer appeared five days after intercourse with a prostitute. A bilateral tender inguinal adenitis was present, the glands being from the size of an olive to that of small hen's egg. The patient stated that the adenitis appeared a day or two before he noticed the penile ulcer. There was a slight urethral discharge, which was present throughout. The ulcer and adenitis remained about the same for from four to five weeks. About the beginning of the fifth week the penile ulcer began to enlarge, and a massive edema of the prepuce appeared. The first Frei test gave negative results. Each of the remaining tests showed an increasing reaction. No Ducrey bacilli were found, and smears showed no gonococci. Repeated dark field examinations for *Spirochaeta pallida* gave negative results. The Wassermann reaction of the blood was positive on Feb 7, 1936 (about the seventh week after the onset of the adenitis), and a macular eruption of secondary syphilis appeared on the skin at that time.

LYMPHOGRANULOMA VENEREUM Presented by DR JOHN F MADDEN, St Paul

Mrs J R, aged 25, first complained of a painful induration and edema of both labia majora and of an inguinal adenitis on the left side on Nov 20, 1935. She was first seen at the hospital on Dec 6, 1935, when the gland was incised and drained. There was no history or evidence of a primary ulcer. The patient had had sexual intercourse with her husband shortly before the edema and adenitis were noted. The husband had a penile ulcer and inguinal adenitis at that time. The Wassermann reaction of the blood was repeatedly negative. Several smears showed no gonococci or Ducrey bacilli. The Frei reaction was moderately positive on Dec 8, 1935, and it has been strongly positive since Jan 1, 1936.

LYMPHOGRANULOMA VENEREUM Presented by DR JOHN F MADDEN, St Paul

J R, a laborer aged 30, was first seen on Oct 1, 1935, at which time he presented a painful fluctuant inguinal bubo on the left side and a pea-sized painless ulcer of a week and a half duration on the middle of the dorsal aspect of the prepuce. There was also a bean-sized, firm nodule to the left of the midline about half-way up the shaft of the penis. The patient stated that he noticed a urethral discharge about one month previously and that this was followed in a few days by the inguinal adenitis. The bubo was incised, but the disease continued to progress until the patient was admitted to the hospital on Dec 17, 1935. Repeated dark field examinations of material from the ulcer gave negative results for spirochetes. No gonococci or Ducrey bacilli were found on repeated examinations. The first Frei test on November 26 gave a positive reaction, and since then there has been a more marked reaction to each test.

DISCUSSION

DR R J BAILEY, Rochester (by invitation) At the Mayo Clinic my co-workers and I have attempted to make comparative studies with the various Frei antigens. Dr Welsh recently obtained from Dr J Tamura Frei antigen, cultured virus of lymphogranuloma venereum and antilymphogranuloma venereum serum. In the few patients on whom we have made comparative intradermal tests the cultured virus gave the most marked reaction. Tamura Frei antigen, Cook County Frei antigen (furnished by Dr Wien) and Lederle Frei antigen all gave positive results but to a lesser degree.

In one case, that of a young man from South America who had a marked stricture of the rectum of several years' duration, desensitization was started with the Cook County antigen. Within three weeks improvement proceeded to the point where a proctoscope could be inserted. This brings up the point, which has been verified by postmortem examination, that the stricture is not entirely cicatricial but is caused in part by the marked round cell infiltrate, the latter infiltrate may resolve as a result of biologic therapy.

The virus has been cultivated through several animal passages by Dr Tamura.

DR HAMILTON MONTGOMERY, Rochester I wish to emphasize what Dr Michelson has already said, namely, that not all lesions in the groin or axilla are to be regarded as caused by lymphogranuloma venereum. At one time false positive reactions to the Frei test were obtained.

A patient presented at a recent meeting of the Chicago Dermatological Society exhibited a condition which clinically was at first suspected of being lymphogranuloma venereum with involvement of both axillae, the groin and other regions, but further investigation proved that the disease was extensive tuberculosis.

DR JOHN F MADDEN, St Paul My co-workers and I made several interesting observations on our patients with lymphogranuloma venereum. Two of the patients noticed a urethral discharge from one to two weeks before the inguinal adenitis appeared. Although the discharge was examined repeatedly, no gonococci were ever found. We attempted desensitization with antigen, roentgen therapy, intravenous administration of neoarsphenamine and medication with antimony and potassium tartrate in conjunction with incision and drainage of the fluctuant buboes.

As long as our patients were ambulatory no form of treatment seemed to benefit them. When they were kept in bed and treated with hot packs and small doses of filtered roentgen radiation steady improvement occurred.

CONTACT DERMATITIS FROM OVERSHOES Presented by DR JOHN F MADDEN,
St Paul

LIPEMIA-XANTHOMA Presented by DR D D TURNACLIFF, Minneapolis

H B, a man aged 23, whose height is 5 ft 2½ inches (1.59 meters) at present weighs 157 pounds (72 Kg). Four years ago he weighed 183 pounds (83 Kg). He has lichen simplex chronicus on his left leg, this is not associated with the condition because of which he is presented.

The patient has always been of the same stature and "gets fat" easily. He is the only member of his family who exhibits this tendency.

About three years ago there developed three lesions of xanthoma on the right palm and right foot. At about that time the patient was advised to reduce, and he gradually took off weight until he weighed 150 pounds (68 Kg). The lesions remain stationary. When I first saw the patient six weeks ago I suggested that he increase his weight 4 or 5 pounds (1.8 or 2.3 Kg) before an examination of the blood was made. One week ago examination gave the following results: lipoids, 1,360 mg; cholesterol, 603 mg; and sugar, 107 mg per hundred cubic centimeters of blood.

This is about twice the normal amount. To make sure that the results did not represent a normal increase in fat content of the blood due to increase in weight, I recently examined blood from an obese man weighing 280 pounds (127 Kg) who had gained 30 pounds (13.6 Kg) in four weeks, and the lipid content of his blood was normal.

Further evidence of pituitary disorder is the fact that in this man the growth of hairs associated with sexual development is lacking, although his genitalia are normal.

DISCUSSION

DR CARL W LAYMON, Minneapolis. Little is actually known concerning the pathogenesis of xanthoma. The lesions may occur in persons having increased cholesterol content of the blood or in persons having a normal amount of cholesterol. Increase in lipid content of the blood does not necessarily parallel gain in body weight.

DR HAMILTON MONTGOMERY, Rochester. Dermatologists tend to narrow the concept of xanthoma. There are all types of xanthomatosis, including also the Schiller-Christian syndrome. Xanthomatous lesions may be seen in the larynx and pharynx, even independently of any cutaneous manifestations. They should be searched for whenever the question of xanthomatosis of any type arises.

DR D D TURNACLIFF, Minneapolis. When the patient weighed about 180 pounds he probably had a marked excess of lipid in the blood. It is my impression that patients with this disorder have so much lipid in their blood serum that it crowds through the capillaries.

The members may remember that last year I presented a man with several hundred lesions of xanthoma which cleared up completely when the fat content of the blood was reduced through dieting (*ARCH DERMAT & SYPH* 33:898 [May] 1936, 34:320 [Aug] 1936). It is conceivable, if a lesion of xanthoma persists for some time, that enough fibrosis takes place so that a reduction of the fat content of the blood will not cause the lesion to recede.

Would it not be conceivable that diabetic patients go through a period of lipemia and that the lesions of xanthoma develop during that period?

I was glad to have the opportunity to check the lipid content of the blood on the man weighing 280 pounds because the results of that examination will perhaps classify the lipemia group more definitely with dysfunctions of fat metabolism.

LOS ANGELES DERMATOLOGICAL SOCIETY

THOMAS W NISBET, M D, *Secretary*

Feb 9, 1936

NELSON PAUL ANDERSON, M D, *Chairman*

DISSEMINATED LUPUS VULGARIS Presented by DR SAUL S ROBINSON

XANTHOMATOSIS Presented by DR STANLEY CHAMBERS

The patient's illness dates back about three years. At that time a swelling in the legs was noticed, swelling of the forearms and upper portions of the arms gradually developed, later the tissues of the face, chest and back became involved. There has been some loss of function of the hands associated with the tumor-like masses on the forearms. The patient states he has been treated in several clinics and by private physicians since the condition was first noted.

There is a yellowish plaquelike waxy infiltrative involvement of the entire head, which is more marked over the supra-orbital areas of the forehead and the bridge of nose. The same type of involvement is present in the areas generally affected by seborrhea, the anterior aspect of the sternum, the back and the arms. There are several hard masses on the forearms and upper portions of the arms.

On Jan 7, 1936, the Wassermann reaction of the blood was negative, and chemical examination of the blood gave the following results: nonprotein nitrogen, 38.7 mg per hundred cubic centimeters, urea nitrogen, 19 mg, sugar, 102.6 mg, calcium, 11.8 mg, and cholesterol, 151.5 mg. The icteric index was 13.8. The van den Bergh reaction was negative.

On Jan 6, 1936, the report on a roentgen examination was as follows: There was no evidence of pathologic changes in the right and left forearm and wrist. There were no apparent calcium deposits within the soft tissue.

The biopsy report stated that the specimen consisted of a piece of skin from the forehead, the epidermis of which did not show. The dermis, however, contained islands of polyhedral cells and oval cells, rather closely placed, with a comparatively small nucleus, eccentrically placed. The cytoplasm was foamy. The cells were probably endothelial leukocytes. There was an occasional giant type cell. The diagnosis based on microscopic examination was xanthoma.

DISCUSSION

DR SAUL S ROBINSON: I suggest the diagnosis of leprosy. There seems to be muscular atrophy.

DR C R HALLORAN: The clinical picture is that of leprosy. I suggest that further studies be made with this thought in mind.

DR MOSES SCHOLTZ: If the diagnosis is correct, this is an interesting case. My first suspicion was leprosy, a diagnosis which, I think, should be considered. "Xanthomatosis" is not a clear term. Does it mean degeneration of the skin or toxic xanthoma? The lesions are entirely too superficial and too extensive to represent degeneration of the skin. In many places there is wrinkling of the skin. I suggest an alternative diagnosis of chronic dermatitis atrophicans with secondary xanthomatous deposits.

DR IRVING R BANCROFT: I think that the diagnosis of leprosy should be considered.

DR H C L LINDSAY: I noticed that one eyebrow was partly missing, but it would take time to make a definite diagnosis.

DR KENDAL FROST: I agree with Dr Scholtz. I should not presume to question the diagnosis after the extensive investigation which has been made. The clinical picture is different from any type of xanthoma which one ordinarily sees and is interesting.

DR WILLIAM H GOECKERMAN Dr Frost has expressed my opinion I understand that the case has been studied thoroughly If xanthomatosis proves to be the correct diagnosis, a report of the case ought to be sent to the international congress

DR SAMUEL AYRES JR I have never seen any clinical picture like the one in this case I agree with the remarks which have been made, and I second the suggestion that the patient may present xanthomatous changes associated with some other disorder Whether leprosy could produce that change, I do not know, but clinically that diagnosis is the first thing suggested by the patient's appearance There are areas of definite infiltration of a sclerodermatous type as well as areas of atrophy where the skin is like tissue paper and atrophic in appearance Certainly the case is highly interesting

DR STANLEY CHAMBERS Xanthomatosis is, of course, a pathologic entity which is probably better understood by biochemists and pathologists than by dermatologists My conception of the disease has always been a clinical one, yet if one appreciates step by step the pathogenesis of the disease, the picture which this patient exhibits becomes logical and makes one wonder why it is not seen more frequently I know of no other disease which produces the pathologic changes so evident in this case Xanthoma or foam cells are pathognomonic of the disease The sections presented tonight show great numbers of these characteristic cells Repeated examination of nasal smears showed no evidence of leprosy Dr Paul O'Leary and his associates at the Mayo Clinic studied this case The diagnosis at that time was xanthomatosis

DERMATITIS FACITIA Presented by DR MOSES SCHOLTZ

MANHATTAN DERMATOLOGICAL SOCIETY

MIHRAN B PAROUNAGIAN, M D, *Secretary*

Feb 11, 1936

PAUL E BECHET, M D, *Chairman*

A CASE FOR DIAGNOSIS (ERYSIPELOID?) Presented by DR FRED WISE

G R, a boy aged 10 months, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital because of a recurrent eruption of seven weeks' duration The present attack occurred about five days ago The previous history, including that of birth and past illnesses, is essentially irrelevant

The eruption is widespread and involves the buttocks, lower extremities, hands, feet and prepuce The pubic region and groins are not affected, but a band about 6 inches (15 cm) wide spreads across the entire width of the abdomen The affected parts are diffusely erythematous, slightly edematous, dry and in some parts, especially on the lower portion of the back and on the abdomen, covered with dry adherent thin lamellar scales The other areas are quite shiny and sharply margined There is no photophobia, polyneuritis or paresthesia. There is a daily rise of temperature to 101 F, coincident with a flare-up of the eruption The rash is said to vanish almost completely every day and to reappear at fairly regular daily intervals The sharp margin of the eruption on the abdomen seems to coincide with the upper edge of the adjusted diaper The thenar regions of both palms exhibit sharply margined flat smooth and glistening patches of dermatitis, and the soles are similarly affected, except that the dermatitis involves the entire plantar surfaces

DISCUSSION

DR ANDREW J GILMOUR If the child had more fever I might suggest the diagnosis of an erysipeloid eruption

DR MIHRAN B PAROUNAGIAN I have never seen any disorder like that before, so I cannot make a diagnosis

DR LUDWIG OULMANN The disorder may be an allergy to alkaline substances Acrodynia can easily be excluded, and an erysipeloid condition would be deeper seated

DR HOWARD FOX Some of the lesions on the soles suggest a diffuse syphilid, but the rest of the eruption does not at all resemble that disease, and I think it can be excluded If it were not for the lesions on the hands, erythema gluteale might be considered

PERIVASCULITIS NODULARIS NECROTICANS Presented by DR FRED WISE.

F M, a woman aged 27, from the clinic of the French Hospital first complained of her cutaneous trouble last December, when she was exposed to cold weather The lower third of the right leg, chiefly the frontal and lateral aspects, presented a series of from twenty-five to thirty well defined flat discoid soft nodules, varying in size from that of a pea to that of a dime and showing a range of color from light pink to violaceous Some of the lesions exhibited faint superficial erosions in their centers They were painful and tender The intervening skin was cyanotic and cold

The patient had infantile paralysis in childhood, and she wears a brace on the affected leg On the external surface of the right heel and outer malleolus is an elongated postoperative scar resulting from a bone graft performed in an attempt to correct her disability

Her general health is said to be quite normal There are no clinical evidences of active tuberculosis and no other cutaneous lesions Tests with tuberculin will be made later

DISCUSSION

DR LUDWIG OULMANN From a purely clinical standpoint periphlebitis nodularis necroticans cannot be differentiated from a possible tuberculid, a biopsy and tuberculin tests are necessary to establish the diagnosis

DR MIHRAN B PAROUNAGIAN Clinically I should agree with Dr Oulmann's suggestion that the disease may be tuberculid

DR. PAUL E BECHET In my opinion the disorder belongs to the tuberculid group The fact that it occurs only on one leg does not refute such a diagnosis The lesions are on the deformed and shrunken leg and may well have developed there because of the lowered resistance of the leg to infection or disease as well as because of a lowered circulation Is periphlebitis nodularis necroticans a clinical entity, or is it an atypical type of Bazin's disease? Certainly some of its manifestations are entirely different from those of erythema induratum or any other known dermatosis Some years ago I observed two cases of an exactly similar clinical syndrome, namely, subcutaneous nodules or small tumors arranged in beadlike formation on the lower third of the leg The nodules were deep and hard and did not fluctuate They were reddened but not painful and seemed attached to the subcutaneous tissue They did not break down, but in the course of several months disappeared, leaving a brownish discoloration and a depressed area They did not resemble Boeck's sarcoid in the least, nor could they be regarded as lesions of erythema nodosum

FAVUS OF THE SCALP AND NAILS Presented by DR FRED WISE

L S, a woman aged 24, an accountant, was born in the United States Her eruption began on the scalp eighteen years ago The patient had two epilations with roentgen rays ten and four years ago, respectively The eruption involving the fifth finger-nail of the right hand and that involving the third finger of the

left hand began three and two years ago, respectively. The patient received ten treatments with roentgen rays to the affected nails one year ago.

There is a grayish yellow discoloration affecting the aforementioned nails together with a moderate subungual hyperkeratosis. The nail of the left middle finger is broken off at about the middle. The distal portion of the nail bed is grayish white. There is a severe grade of alopecia affecting the entire scalp, it is most marked over the central portion and is associated with moderate scaling. The scrapings as well as the cultures from the finger-nails and from the scalp showed the organism of favus.

The Wassermann, Kahn and Kline tests were negative.

A CASE FOR DIAGNOSIS (LUPUS ERYTHEMATOSUS?) Presented by DR. ANDREW J. GILMOUR

E. H., a man aged 25, single, born in Ireland, is an attendant in a hospital. He has always been well except for the fact that he had lichen planus in 1932. The trunk and extremities were extensively involved, and on these locations pigmentation remained several months. The mouth was slightly involved.

Since it first became involved the mouth has never been quite normal. There has been a blue-red color extending back from the angles of the mouth. These two lines followed the approximation of the teeth for 1 inch (2.5 cm) on each side of the mucous membrane of the mouth. This line was from $\frac{1}{2}$ to $\frac{3}{4}$ inch (1.2 to 2 cm) in width, level with the surface and not ulcerated. No sensation to food was elicited. The teeth were not rough.

Since the middle of December 1935 there have been on the right side of the exposed portion of the mucous membrane of the lower lip two slightly raised hyperkeratotic lesions each $\frac{1}{2}$ inch in diameter. These have been scaly and gray, they were never ulcerated or covered with scabs.

The Wassermann test was negative.

DISCUSSION

DR. FRED WISE: I think that this eruption is lupus erythematosus.

DR. HOWARD FOX: I agree entirely with Dr. Wise, and I can see no reason for considering the disorder an epithelioma. I suggest treatment with a gold preparation.

LUPUS ERYTHEMATOSUS Presented by DR. HOWARD FOX

D. D., aged 35, a Negro, has suffered from a lesion on the scalp for the past three years. On the vertex is an oval patch about 7 inches (18 cm) in the longest dimension, which is red, dry, atrophic and devoid of hair. Since the patient was admitted to the hospital he has had frequent crops of flaccid bullae on the affected area. No cause for these eruptions has been found.

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Feb 21, 1936

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DERMATITIS MEDICAMENTOSA DUE TO BARBITURATE Presented by DR. JOHN B. LUDY

H. J., a woman aged 37, presents an outbreak of small papules on a purpuric background. She states that she took sleeping tablets (dial) after a severe emotional upset. Four days ago a generalized pruritic eruption appeared suddenly. The patient's skin is purplish in cold weather. There is no history of rheumatic fever, tuberculosis or other infections. There is marked dental sepsis.

DISCUSSION

DR MARION B SULZBERGER, New York I think that one of the main things to remember about eruptions due to drugs is that they can take all forms, no matter what the drug is that causes them. The typical eruptions are only those which are most frequently caused by one certain drug. In other words, while the most common eruption due to phenolphthalein is the fixed eruption, that drug does not necessarily cause only fixed eruptions. Bromides may cause not only acneiform or fungating, but also eczematous, seborrheic and occasionally fixed eruptions. In this case I think that it is difficult to make a differential diagnosis between an eruption due to bromide and one due to barbiturate. I understand that the patient has taken both drugs. The fact that many of the lesions are follicular makes me suspect that the causative drug may be a bromide, it is known that eruptions due to bromides are often follicular. There are acneiform lesions on the chest, back and face, which would point more to a halogen as the cause of the eruption, and hemorrhagic and purpuric eruptions such as that exhibited by this patient may develop from ingestion of bromides. Therefore, while it is possible that the barbiturate may have caused all the lesions, I think that the bromide must be considered also.

DR JOHN H STOKES In commenting on eruptions due to a drug I always say that that diagnosis is a last rather than a first resort. One should carefully eliminate every other explanation before one attempts to incriminate a drug. I think that rule should be applied even in the case of drugs which are known to produce distinctive and characteristic eruptions because I have seen some of the most egregious mistakes made in dermatologic practice by systematically attributing eruptions which follow intake of drugs to the drugs. I do not think there is any worse *post hoc ergo propter hoc* practice than the tendency to call an eruption which appears after a patient receives a drug an eruption due to a drug. Purpura is due to a drug only when it is proved to be so, and a painstaking and systematic study of this patient's disorder should be made before it is called an eruption due to barbiturates, bromides or any other drug. There prevails at present an epidemic infection of some sort which manifests itself in a large number of persons by gastro-intestinal disturbances and which, I am convinced, is causing a flare-up of pyogenic infections of the skin by a sensitizing process. I think that infection will be responsible for some toxic erythemas. I should not be at all surprised if in some cases purpura results from it. The fact that a person is taking a barbiturate at the time a purpura appears does not justify a diagnosis of eruption due to a drug.

DR WILLIAM O ROOP, Atlantic City, N. J. The eruption on this patient's face is an acne rosacea, and she admits that this eruption was present for quite a long time before the generalized eruption which now involves the body. In my opinion the eruption on the body resembles more an eruption due to barbituric acid than one due to a bromide.

DR EDWARD F CORSON It seems to me that the sudden onset and the generalized distribution point to barbituric acid rather than to bromide as a cause.

A CASE FOR DIAGNOSIS (NEURODERMATITIS? PREMYCOTIC STAGE OF MYCOSIS FUNGOIDES?) Presented by DR LOUIS GOLDSTEIN

H. L., a man aged 26, presents a generalized eruption of a patchy, papular and desquamating character varying in shape, color and process of involution. Certain parts show definite infiltration, especially at the upper part of the thighs and in the region of the axillae, where there are distinct ribbon-like raised borders. The inguinal glands are markedly enlarged. A moderate pruritus is present more or less constantly. The condition has been present for three months. It began on the legs as a papular dermatitis after the patient wore woolen stockings (contact dermatitis?) and rapidly progressed to the rest of the body. Early in the course of the disease the dermatitis of the legs developed into an inflammatory edema with exudation, while the rest of the body presented a purplish papulation which

gradually formed various-shaped patches as well as extensive desquamation. About seven weeks ago there appeared on the chest and trunk papular lesions suggestive of a superimposed pityriasis rosea. These became confluent and finally evolved into the stage of dermatitis existing at present. The Wassermann reaction of the blood was negative. Chemical examination of the blood gave normal results. The blood count showed a moderate leukocytosis, the number of leukocytes being 10,000, and a corresponding increase of polymorphonuclear leukocytes. Urinalysis gave negative results.

DISCUSSION

DR FRANK C KNOWLES I cannot diagnose this eruption.

DR FRED D WEIDMAN I cannot make a diagnosis at present. I think that the case will have to be investigated.

DR FRANK C KNOWLES Some of the lesions certainly resemble *tinea imbricata*. I think further studies in regard to fungous origin should be made.

DR FRED D WEIDMAN I do not believe that the disorder is *tinea imbricata* or generalized dermatophytosis, it is more probably *mycosis fungoides*. Neurodermatitis can be definitely excluded.

DR MARION B SULZBERGER, New York I cannot make a diagnosis either. Naturally, the first thing one thinks of on seeing the isolated patches is a *tinea*, and I think that this diagnosis must be excluded by repeated careful mycologic examination. I have seen recently a *tinea* resembling this patient's eruption, in that case there was generalized lymphadenopathy, and the fungi could be demonstrated. On the other hand, in a case of an eruption somewhat similar to that presented by this patient repeated examinations for *tinea* gave negative results. I do not believe that neurodermatitis need be considered, I do not know what type of neurodermatitis this could be. The way the eruption has spread from the calves, the fact that the lesions are fairly uniform, that the eruption is nonhemorrhagic and that it always spreads centrifugally suggest *tinea* which is becoming generalized. I do not think that *mycosis fungoides* ever starts in one place and spreads from there. As a rule, in *mycosis fungoides* there are multiple lesions beginning in various parts of the skin.

DR J M SCHILDKRAUT, Trenton, N J I think that possibly the disorder is a type of leukemia.

DR SIGMUND S GREENBAUM On morphologic grounds I should diagnose it as plain eczema. I do not know whether it is a premycotic eczema or whether it is due to a chemical from within or without or to a parasite, but the picture now is that of a straight eczema. I must confess, however, that I incline quite strongly to the belief that the eruption is due to a fungus. I think Dr Sulzberger has summarized the arguments cogently for that diagnosis. It is known, however, that in scrapings the organism may not be found even though morphologically there may be evidence of a fungous eruption.

DR LOUIS GOLDSTEIN I wish to ask Dr Sulzberger if the patient would have so much itching and such extensive scaling from a fungous infection.

DR MARION B SULZBERGER, New York My experience is that these generalized atypical fungous infections are often atypical in more ways than one. It is not at all unusual for severe itching to occur in a fungous infection. I have seen cases of fungous infections of the feet in which itching was the outstanding symptom. As far as the scaling is concerned, in cases of widespread involvement the patches often do not come to full development but remain scaling. I think that the entire picture in this case could well be of fungous origin, but this diagnosis requires confirmation by laboratory examination.

DR JOHN H STOKES I should like to point out that itching is much like pain in that it is a function of the individual threshold of sensory responsiveness. Some persons may have itching due to a lesion between the toes and tear themselves frantically, while others may have an extensive eruption of which they are

quite unaware That is apparent in cases of scabies The threshold of itch in scabies varies with the patient and not with the extent or character of the disorder I remember the case of a physician with a typical mycosis fungoides, annular infiltrated lesions were developing, and the patient had had the premycotic stage for eighteen years, but he swore that he had never had any itching Such observations are familiar I think one becomes convinced after a while that itching is a function of the individual nervous system and of the individual reactivity quite as much as, if not more than, of the eruption

A CASE FOR DIAGNOSIS (CHRONIC APHTHAE? ERYTHEMA MULTIFORME?) Presented by DR HERMAN BEERMAN

G S, a man aged 33, was presented at the October 1935 meeting of the society (ARCH DERMAT & SYPH 33:760 [April] 1936) Aside from the oral lesions he has two small ulcers on the scrotum The diagnoses of chronic aphthae, eruption due to phenolphthalein and erythema multiforme have been considered

The differential blood cell count showed 7,200 white cells with 63 per cent polymorphonuclears, 30 per cent lymphocytes, 3 per cent monocytes, 1 per cent eosinophils and 3 per cent transitional forms Urinalysis gave negative results Serologic tests of the blood gave negative results on three occasions A smear from the tongue showed no spirilla, but there were some small round bodies resembling yeasts which may have been mouth contaminants The Pels-Macht test showed a phytotoxic index of 65 The patient was treated with brewer's yeast, 10 drops of dilute hydrochloric acid three times a day, 60 grains (0.39 Gm) of calcium lactate three times a day, sodium perborate locally and five injections of whole blood He received eight injections of neoarsphenamine from Oct 1 to Dec 2, 1935, the first dose being 0.3 Gm and the following doses 0.45 Gm During observation of the patient several lapses were noted After initial improvement had occurred, on Aug 20, 1935, the patient reported that two days previously he had had a rather marked exacerbation of lesions in the mouth and on the scrotum This relapse lasted about two weeks After three weeks of relative freedom from complaints, on September 24, several eroded ulcers were noted on the scrotum and penis During the time neoarsphenamine was given it seemed that there was marked improvement, but on December 2, the date of the last injection, two new ulcers appeared, one on the left side of the buccal mucosa and one on the palate

DISCUSSION

DR SIGMUND S GREENBAUM I have recently observed several cases, and there have been a number reported in the literature, in which these chronic aphthae have been the result of an idiosyncrasy for certain foods I suggest that the patient be tested with food allergens though the results are likely to be negative, or that he be put on an elimination diet—the latter procedure is usually more successful

DR JOHN H STOKES I may point out that one way of achieving a result in a supposedly allergic process of this sort seems to be to increase the intake of vitamins, especially that of vitamin B, which has a therapeutic effect and an influence on intestinal infection and intestinal absorptive power That treatment was used coincidentally with the neoarsphenamine, and yesterday my co-workers and I agreed that we were not sure whether the vitamins or the neoarsphenamine had caused the improvement Improvement as a result of treatment with neoarsphenamine was much greater than it had been as a result of the combined therapy, however, and consequently we were inclined to think that the arsenic had made some difference But certainly the allergic background should be investigated

DERMATITIS HERPETIFORMIS Presented by DR JOHN B. LUDY

D H, a man aged 44, says that eighteen months ago a red slightly scaly eruption appeared on one knee and shortly spread, slightly involving the buttocks, the elbows, the dorsal aspect of the arms and the shoulders In June 1935 the character of the eruption changed abruptly with the onset of a vesicular eruption

similar to the existing outbreak. There were violent itching and burning. Arsenic controlled the eruption for a number of months. On Feb 10, 1936, calcium gluconate was substituted for the arsenic. On the evening of February 11 the patient went to a dance but ingested nothing but chocolate cake and nonalcoholic punch. The next morning there was a profuse eruption which was symmetrical and consisted mostly of bullae and of an erythema multiforme type of outbreak with festooned and circinate lesions, best exemplified in the region of the groins and on the lower portion of the back. Some of the latter lesions are of the herpes iris type. The axillae are crowded with vesicles. The face has been involved only in the recent attack. There are no lesions on the mucous membrane. The patient had carbuncles five years ago. His tonsils have not been removed. He has no sinus trouble, is not constipated and has no gastro-intestinal disorder.

DISCUSSION

DR SIGMUND S GREENBAUM. Over a great part of the body the patient presents sheets of urticarial-like eruption in addition to the bullae and hemorrhagic blebs. There are no individual wheals such as are common to urticaria, and there is no real herpete arrangement. The last case of this disorder I saw was in Darier's clinic, it was presented as a form of painful polymorphous bullous dermatitis of Brocq, which condition, of course, is now grouped entirely under the heading of dermatitis herpetiformis.

DR FRANK C KNOWLES. My co-workers and I have followed this patient for about five years. He has taken arsenic, but he seemed to have a certain idiosyncrasy for the drug and had to stop taking it. Some improvement from intravenous administration of calcium gluconate is becoming manifest.

DR MARION B SULZBERGER, New York. In my opinion this is undoubtedly a case of Duhring's disease with, as Dr Greenbaum has said, polymorphous lesions. I think the large circinate, sharply circumscribed lesions are interesting on account of the possible connection between Duhring's disease and erythema annulare centrifugum of Darier. Recently several articles have been published which tend to prove that in cases of typical forms of Darier's erythema bullae sometimes develop and that there is probably a connection between Duhring's disease and Darier's annular erythema.

DR JOHN H STOKES. I feel as the other members do, that there is an intermediate picture of erythema multiforme, dermatitis herpetiformis and pemphigus, and I should like to point out one or two differential considerations which, I think, need to be gone into rather fully. In the first place, eruptions like the one exhibited by this patient may be produced by barbiturates. The eruption has been present for five years, during which time the patient has probably taken nearly every drug available. I think one should not forget the possibility of bullous lichen planus and bullous lupus erythematosus in disorders of this sort. If the eruption involved the extremities a little more I should give the latter diagnosis serious thought. The fact that this condition has been present for five years puts it in a group in which I have always been rather interested. I heard after I had seen the first case of this disorder that it had subsequently cleared up as a result of treatment with thyroid, and I suggest that this patient be given as much thyroid as he tolerates. Why thyroid caused the condition to clear up in my patient, I do not know, but on reliable authority I know that she has been nearly free from the disorder for five years, and she told me herself that she had been vastly improved as a result of the treatment.

DR FRED D WEIDMAN. Dr Sulzberger anticipated my remarks. I wish to call attention also to the overlapping of the manifestations with those of erythema multiforme, to the remarkable symmetry of this eruption. It is true, Duhring's disease is roughly symmetrical, but I think it is not quite so strikingly symmetrical as this. A similar problem arose in the case of a patient who had made the rounds of the dermatologists in Philadelphia for many years and whose disorder had been diagnosed as Duhring's disease. He died in the Philadelphia General Hos-

pital The terminal stage of his eruption was of the order of that exhibited by Dr Ludy's patient, i e., of the character of erythema perstans The bullae presented by this patient were lacking, there were only vesicles At necropsy bronchiectasis was demonstrated in both lungs I think that the possibility of a focal infection should be considered in this case

PATCHY ALOPECIA OF THE SCALP DUE TO LICHEN PLANUS Presented by DR REUBEN FRIEDMAN

S R., a woman aged 30, presents on the scalp, particularly over the anterior half, a number of pinkish, slightly scaly patches of alopecia of irregular size and shape The hair all over the scalp can be easily extracted On the trunk and upper extremities there is a generalized eruption of lichen planus, the follicular variety predominating The lower extremities are involved to a less degree The patient reports that a sudden eruption of reddish papules resembling goose flesh was first noticed on the abdomen on Jan 11, 1936 This rapidly spread to the rest of the trunk and to the extremities Two weeks later the patient noticed that she was losing much of her hair Small bald spots were observed early in February The Wassermann reaction of the blood was negative

DISCUSSION

DR SIGMUND S GREENBAUM I think Dr Stokes was the first to present a case of this disorder—lichen planopilaris with cicatricial alopecia—before the society I presented a case of a similar disorder some time ago as one of tuberculid with cicatricial alopecia The patient's cutaneous condition cleared up as a result of treatment with gold sodium chloride, but the alopecia was, of course, permanent Could the condition of the scalp be an acute form of sclero-atrophic lichen planus?

DR JOHN H STOKES I think that this disorder falls within the group which Graham Little illustrated by three cases I should like to see somewhat more typical lesions of lichen planus, but I did see some lesions resembling those of that disease on the abdomen If, as in the case that I showed, one could see typical lesions and Wickham's striae about the wrists, I should feel more at ease about the diagnosis, but I have seen lichen planus so extensively follicular and yet so definitely lichen planus that I do not see why this patient's eruption is not within the range of variation of lichen planus

DR MARION B SULZBERGER, New York I agree with Dr Stokes I have seen a few cases of the disorder which Graham Little called lichen spinulosus with folliculitis decalvans and which is now termed lichen planus et acuminatus atrophicans I have seen cases in which it was interesting to note that one could see at first spinous lesions on the scalp resembling those on the body and that these follicular lesions preceded the diffuse and scarlike alopecia Probably the same follicular process seen on the glabrous skin without alopecia leads to the alopecia on the scalp I do not know what the prognosis is for these lesions on the scalp, they certainly do not look as if hair would grow on the involved areas

DR JOHN H STOKES In a patient whom I have seen for five years the alopecia has been permanent

DR REUBEN FRIEDMAN I think that some of the lesions, particularly those on the flanks, are definitely lichen planus The entire eruption began in the manner of an acute goose flesh-like eruption, to use the patient's expression I think that it was a lichen planus of a follicular type and that some of these follicular lesions eventually developed into the typical flat lichen planus The patient has also lesions slightly suggestive of lichen planus on the buccal mucosa

Book Reviews

Deliberationes Congressus Dermatologorum Internationalis IX-1 Budapest, 13-21 Septembris, 1935 Pp 1005

This book is an exceedingly interesting report of the proceedings of the congress. It gives the papers and discussions classified under the nine themes of the congress, as follows: (1) new investigations of the functions of the skin, (2) reciprocal relations and antagonisms between the skin and the internal organs, (3) allergy in dermatology and syphilology, (4) metabolic disturbances in cutaneous diseases, (5) effect of external causes on the frequency and form of cutaneous diseases, (6) the filtrable viruses in cutaneous diseases, (7) new results of the investigations of the pathology of tuberculosis, (8) therapy of syphilis, (9) criteria of the sanitation of syphilis.

The various titles indicate the comprehensiveness and fulness of the discussions of these formal themes. Over 400 pages are devoted to this section of the book, and the reports and discussions come from outstanding workers.

The second section is devoted to special papers given in conference and in meetings devoted to particular subjects, namely, conference on comparative dermatology, individual dissertations which are grouped under physiology, general pathology, general therapy, physical therapy, lymphogranuloma venereum (lymphogranulomatosis inguinalis), leprosy, tropical diseases, bacteriology and mycology, psoriasis and parapsoriasis, pathologic conditions of the hairs and nails, tumors, syphilis, gonorrhea and various unclassified papers.

The whole book comprises 1,005 pages. It is a magnificent exposition of the present state of knowledge in the field of dermatology.

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NOVEMBER 1936

**PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH
DEARBORN STREET, CHICAGO, ILLINOIS ANNUAL SUBSCRIPTION, \$8 00**

Entered as Second Class Matter, Oct 30, 1917, at the Postoffice at Chicago, Illinois,
Under Act of Congress of March 3, 1879
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